

SPECIFICATION

DIHYDROPYRAZOLOPYRIDINE COMPOUNDS AND PHARMACEUTICAL USE THEREOF

TECHNICAL FIELD OF THE INVENTION

5 The present invention relates to new compounds for medicaments, which have a glycogen synthase kinase-3 beta (GSK-3 β)-inhibitory activity, and use thereof.

BACKGROUND OF THE INVENTION

It has been reported that glycogen synthase kinase-3
10 beta (GSK-3 β), a protein kinase, is involved in the causes of various diseases as noted in the following.

Type-II diabetes is a disease in which the insulin reactivity of pancreatic β cells becomes low and glucose in blood increases. As a result, complications such as diabetic
15 nephropathy, retinosis, heart disease and the like are induced. GSK-3 β acts for inhibiting glycogen accumulation in peripheral tissues, lowering insulin response and increasing glucose in blood by phosphorylating glycogen synthase. Lithium having a GSK-3 β -inhibitory activity actually lowers glucose in blood by
20 a GSK-3 β -inhibitory activity (Proc. Nat. Acad. Sci., 93, 8455 (1996)). Therefore, medicaments having a GSK-3 β -inhibitory activity are considered to be a pharmaceutical agent effective for the improvement of Type II diabetes and complications thereof.

25 The developmental mechanism of Alzheimer's dementia has not yet been elucidated. However, it is considered that amyloid aggregation and neurofibril changes are closely related to the cause of the development. GSK-3 β is involved in both the amyloid aggregation and the neurofibril changes as
30 follows. (1) It binds with variant presenilin and increase production of insoluble amyloid (Proc. Nat. Acad. Sci., 95, 9637 (1998)). (2) It causes phosphorylation of the Tau protein, which causes neurofibril changes, and weakens the backbones of

neurons to induce neuronal death (Neurosci. Lett., 128, 195 (1991)). In addition to the above, (3) the direct involvement of GSK-3 β in neuronal death through inactivation of pyruvate dehydrogenase by phosphorylation to decrease the production
5 amount of acetylcholine necessary for maintaining cell activity (Proc. Nat. Acad. Sci., 93, 2719 (1996)) has been reported.

In addition, the effectiveness for AIDS encephalopathia as a neurodegenerative disease other than Alzheimer's dementia
10 has been suggested. Tat, which is a protein produced by HIV virus that causes AIDS, enhances GSK-3 β activity in neurons to induce neuronal death (J. Neurochem., 73, 578 (1999)). From the above, GSK-3 β inhibitors are considered to be medicaments effective for improving neurodegenerative diseases including
15 Alzheimer's dementia.

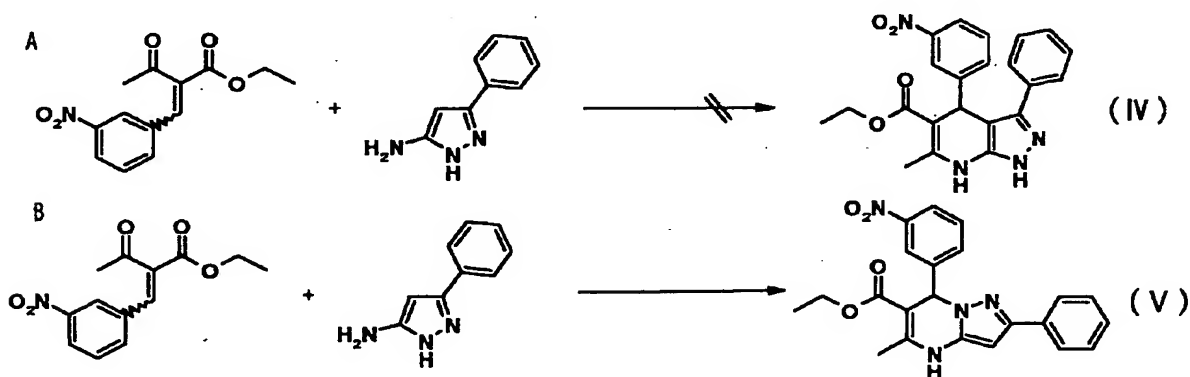
Lithium and valproic acid, which have anti-manic-depressive activity, have a GSK-3 β inhibitory activity (J. Neurochem., 72, 1327 (1999)). The relationship between anti-manic-depressive activity and GSK-3 β inhibitory activity is
20 unclear, but a suppressive activity on glutamic acid toxicity is considered to be partly responsible for maintaining neuronal activity (Proc. Nat. Acad. Sci., 95, 2642 (1998)). Based on the foregoing, GSK-3 β inhibitors are considered to be medicaments effective for improving manic-depressive psychosis.

25 NF-AT, a transcription factor, is dephosphorylated by calcineurin to increase immunological responses (Science, 275, 1930 (1997)). GSK-3 β acts for suppressing immunological function by conversely phosphorylating NF-AT. Therefore, GSK-3 β inhibitors are considered to be medicaments effective for
30 immunopotentialiation.

Incidentally, JP-A-3-272189 (invention drawn to an improved synthesis method of mevalolacton intermediates), JP-A-2-275878 (therapeutic agents for hyperlipoproteinemia and

atherosclerosis) and JP-A-1-272584 (therapeutic agents for hyperlipoproteinemia) disclose pyrazolo[3,4-b]pyridine compounds wherein the 6-position is either methyl, isopropyl or cyclopropyl. These publications do not disclose or suggest
5 any action of these compounds on GSK-3 β or the central nervous system.

The specifications of JP-A-59-65089, JP-A-59-118786, JP-A-60-56979, JP-A-60-197685 and the like disclose 6-methyl-4-substituted phenyl-4,7-dihydropyrazolo[3,4-b]pyridine-5-
10 carboxylate compounds used for the treatment of cardiovascular diseases, and they are produced by similar methods. The present inventors reproduced the following reaction A according to the method described in JP-A-59-65089, but failed to obtain the compound of Example 14 (formula (IV) in the
15 following) described therein. They confirmed that only the pyrazolo[1,5-a]pyrimidine derivative represented by the formula (V) could be produced. They measured IR, NMR and the melting point of the compound of the formula (V) and found them to be identical with IR, NMR and the melting point
20 described in the specification of this publication. It is therefore concluded that an erroneous structural formula has been disclosed in these publications. In other words, 6-methyl-4-substituted phenyl-4,7-dihydropyrazolo[3,4-b]pyridine-5-carboxylate cannot be synthesized according to
25 the methods described in these publications.



The compound of the above formula (IV) can be synthesized according to the method described in J. Chem. Soc., Perkin Trans. 1, 947 (1996), and this publication discloses methyl 4-(2-chlorophenyl)-6-methyl-4,7-dihydro-1H-pyrazolo[3,4-b]pyridine-5-carboxylate and the like.

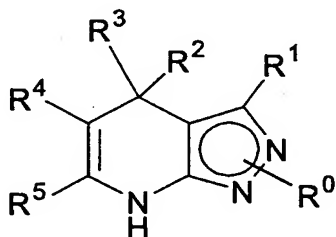
SUMMARY OF THE INVENTION

An object of the present invention is to provide novel compounds having a selective and strong inhibitory activity against glycogen synthase kinase-3 beta (GSK-3 β), and further, medicaments comprising them and pharmaceutical compositions comprising them.

The present inventors have intensively studied to achieve the above object, and have found that 4,7-dihydropyrazolo[3,4-b]pyridine derivatives have a selective and strong inhibitory activity on GSK-3 β , which resulted in the completion of the present invention. That is, the present invention relates to medicaments comprising, as an active ingredient, dihydropyrazolopyridine compounds represented by the following formula (I), which have a GSK-3 β -inhibitory activity and can be used as medicaments, optical isomers thereof, pharmaceutically acceptable salts thereof, or hydrates thereof.

The present invention provides the following.

[1] A dihydropyrazolopyridine compound of the formula (I):



wherein

R⁰ is hydrogen, alkyl, aralkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl,

hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl,
carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl,
alkylsulfonyl, phenylsulfonyl, phenylsulfinyl,
mercaptoalkyl, alkylthioalkyl, acyloxyacetyl,
5 acyloxyalkyl, phenyl optionally having substituent(s),
aromatic heterocyclic group optionally having
substituent(s), phenylalkyl optionally having
substituent(s), or a group of the formula: $-COOR^8$
(wherein R^8 is hydrogen, alkyl, aryl optionally having
10 substituent(s) or aralkyl optionally having
substituent(s));

R^1 and R^2 are the same or different and each is hydrogen, alkyl,
aralkyl, acyl, cycloalkyl, hydroxy, thiol, halogen,
amino, formyl, carboxy, cyano, nitro, alkylthio,
15 haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy,
phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl,
phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl,
aminocarbonyl, alkylthiocarbonyl, carboxyalkyl,
cycloalkoxyalkyl, phenylthio, alkylsulfinyl,
20 alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
alkylthioalkyl, phenyl optionally having
substituent(s), aromatic heterocyclic group or
phenylalkyl;

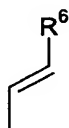
R^3 is
25 (1) alkyl or haloalkyl,
(2) cycloalkyl,
(3) phenyl optionally having substituent(s),
(4) aromatic heterocyclic group,
(5) a group derived from a benzene ring fused with a
30 saturated or unsaturated 5 or 6 membered carbocyclic
ring,
(6) a group derived from a benzene ring fused with a
saturated or unsaturated 5 to 7 membered carbocyclic

ring containing 1 to 3 heteroatom(s), or

(7) a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring,

wherein the groups of (2) to (7) may have one or more substituent(s), or

a group selected from the groups represented by the following formulas (II) and (III):



(II)



(III)

wherein R⁶ and R⁷ are each phenyl optionally having substituent(s) or an aromatic heterocyclic group,

or R² and R³ in conjunction form a ring optionally containing heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);

R⁴ is alkoxy carbonyl, alkyl carbonyl, aminocarbonyl, hydrazinocarbonyl, alkylthiocarbonyl, formyl, carbamoyl, alkylthio, phenylthio, alkylsulfinyl, phenylsulfinyl, alkylsulfonyl, phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, phenyl optionally having substituent(s), an aromatic heterocyclic group optionally having substituent(s), cyano or nitro; and

R⁵ is hydrogen, cyano, formyl, alkyl, cycloalkyl, alkoxyalkyl, phenoxyalkyl, dialkoxyalkyl, hydroxyalkyl, haloalkyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, alkoxy carbonyl alkyl,

alkoxy-carbonyl-ethenyl, aryl optionally having
 substituent(s), an aromatic heterocyclic group or
 phenylalkyl, or a group derived from a 5 to 7 membered
 saturated or unsaturated carbocyclic ring containing 1
 5 to 3 heteroatom(s), which is fused with a benzene
 ring; or
 phenylaminoalkyl,
 acyl,
 acylalkyl,
 10 aminocarbonyl,
 arylaminocarbonyl,
 a saturated or unsaturated 4 to 7 membered
 heterocyclic ring optionally having substituent(s),
 a saturated 3 to 7 membered carbocyclic ring having
 15 substituent(s),
 alkyl substituted by a saturated or unsaturated 4 to 7
 membered ring containing 1 or 2 nitrogen atom(s),
 which optionally has a substituent, or
 a group of the formula: $-(CR^aR^b)_nNR^{11}R^{12}$ wherein n is an
 20 integer of 1 to 4, R^a is hydrogen or alkyl, R^b is
 hydrogen or alkyl, R^{11} is hydrogen, alkyl,
 alkylsulfonyl, phenylsulfonyl, phenylalkylsulfonyl,
 alkylsulfinyl, phenylsulfinyl, phenylalkylsulfinyl,
 alkoxy-carbonyl, phenoxy-carbonyl, phenylalkoxy-carbonyl,
 25 alkyl-carbonyl, phenyl-carbonyl or phenylalkyl-carbonyl,
 and R^{12} is hydrogen or alkyl,
 or R^4 and R^5 in conjunction may form a 5 or 6 membered ring
 optionally containing heteroatom(s),
 provided that when R^0 , R^1 and R^2 are each hydrogen, R^4 is
 30 methoxycarbonyl and R^5 is methyl, then R^3 should not be phenyl,
 2-chlorophenyl, 3-nitrophenyl, 4-carboxyphenyl or 4-
 methoxycarbonylphenyl, and when R^5 is alkyl, then R^4 is not
 alkoxy-carbonyl, alkylsulfonyl, alkylsulfinyl, phenylsulfinyl,

phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, cyano or nitro,

or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

5 [2] The dihydropyrazolopyridine compound of the above-described [1], wherein

R^0 is hydrogen, alkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, 10 carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group optionally having substituent(s), 15 phenylalkyl optionally having substituent(s), or a group of the formula: $-COOR^8$ (wherein R^8 is hydrogen, alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s));

R^1 and R^2 are the same or different and each is hydrogen, alkyl, 20 acyl, cycloalkyl, hydroxy, thiol, halogen, amino, formyl, carboxy, cyano, nitro, alkylthio, haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl, aminocarbonyl, 25 alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group or phenylalkyl;

30 R^3 is
(1) alkyl or haloalkyl,
(2) cycloalkyl,
(3) phenyl optionally having substituent(s),

(4) aromatic heterocyclic group,

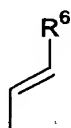
(5) a group derived from a benzene ring fused with a saturated or unsaturated 5 or 6 membered carbocyclic ring,

5 (6) a group derived from a benzene ring fused with a saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s), or

(7) a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3
10 heteroatom(s), which is fused with a benzene ring, wherein the groups of (2) to (7) may have one or more substituent(s), or

a group selected from the groups represented by the following formulas (II) and (III):

15



(II)



(III)

wherein R^6 and R^7 are each phenyl optionally having substituent(s) or an aromatic heterocyclic group,
20 or R^2 and R^3 in conjunction form a ring optionally containing heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);

R^4 is alkoxycarbonyl, aminocarbonyl, hydrazinocarbonyl, alkylthiocarbonyl, formyl, carbamoyl, alkylthio,
25 phenylthio, alkylsulfinyl, phenylsulfinyl, alkylsulfonyl, phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, cyano or nitro; and

R^5 is hydrogen, cyano, formyl, alkyl, cycloalkyl, alkoxyalkyl, phenoxyalkyl, dialkoxyalkyl,

hydroxyalkyl, haloalkyl, carboxyalkyl,
cycloalkoxyalkyl, phenylthio, alkylsulfinyl,
alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
alkylthioalkyl, alkoxycarbonylalkyl,
5 alkoxycarbonylethenyl, aryl optionally having
substituent(s), an aromatic heterocyclic group or
phenylalkyl, or a group derived from a 5 to 7
membered saturated or unsaturated carbocyclic ring
containing 1 to 3 heteroatom(s), which is fused with
10 a benzene ring,

or R^4 and R^5 in conjunction may form a 5 or 6 membered ring
optionally containing heteroatom(s),
provided that when R^0 , R^1 and R^2 are each hydrogen, R^4 is
methoxycarbonyl and R^5 is methyl, then R^3 should not be phenyl,
15 2-chlorophenyl, 3-nitrophenyl, 4-carboxyphenyl or 4-
methoxycarbonylphenyl,
or an optically active form thereof, a pharmaceutically
acceptable salt thereof or a hydrate thereof.

[3] The dihydropyrazolopyridine compound of the above-
20 described [2], wherein R^5 is alkyl having 2 to 8 carbon atoms,
cycloalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, phenyl
optionally having substituent(s), an aromatic heterocyclic
group or phenylalkyl, or an optically active form thereof, a
pharmaceutically acceptable salt thereof or a hydrate thereof.

25 [4] The dihydropyrazolopyridine compound of the above-
described [2], wherein R^1 is hydrogen, alkyl, phenyl optionally
having substituent(s), an aromatic heterocyclic group or
phenylalkyl, or an optically active form thereof, a
pharmaceutically acceptable salt thereof or a hydrate thereof.

30 [5] The dihydropyrazolopyridine compound of the above-
described [2], wherein R^2 is hydrogen or alkyl, or an optically
active form thereof, a pharmaceutically acceptable salt
thereof or a hydrate thereof.

[6] The dihydropyrazolopyridine compound of the above-described [2], wherein R^3 is phenyl optionally having 1 to 3 substituent(s), naphthyl, 2,1,3-benzoxadiazol-4-yl or 3,4-dihydro-2H-benzopyran-8-yl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

[7] The dihydropyrazolopyridine compound of the above-described [2], wherein R^4 is alkoxycarbonyl having 2 to 5 carbon atoms, cyano or nitro, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

[8] The dihydropyrazolopyridine compound of the above-described [2], wherein R^5 is alkyl having 2 to 4 carbon atoms, cyclopropyl, phenyl, thienyl or hydroxyalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

[9] The dihydropyrazolopyridine compound of the above-described [2], wherein R^2 and R^3 in conjunction form a ring containing sulfur atom and the ring is condensed with a benzene ring optionally having substituent(s), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

[10] The dihydropyrazolopyridine compound of the above-described [2], wherein R^0 is hydrogen or a group of the formula: $-COOR^8$ (wherein R^8 is alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s)), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

[11] The dihydropyrazolopyridine compound of the above-described [2], which is selected from the group consisting of (32) ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

- (47) ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (66) ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 5 (73) ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (87) ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (116) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 10 (122) 4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- (140) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- 15 (147) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
- (158) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
- (171) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine,
- 20 (182) ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (183) ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 25 (189) 4-(2-bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- (205) ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (240) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 30 (257) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine,
- (260) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-

isopropyl-2H-pyrazolo[3,4-b]pyridine,

(264) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-

isopropyl-2H-pyrazolo[3,4-b]pyridine, and

(268) 4-(2-bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-

5 dihydro-2H-pyrazolo[3,4-b]pyridine,

a tautomer, an optically active form thereof, a

pharmaceutically acceptable salt thereof or a hydrate thereof.

[12] The dihydropyrazolopyridine compound of the above-described [1], wherein

10 R^0 is hydrogen, alkyl, aralkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, phenylsulfinyl, 15 mercaptoalkyl, alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group optionally having substituent(s), phenylalkyl optionally having substituent(s), or a group of the formula: $-COOR^8$ (wherein R^8 is hydrogen, alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s));

R^1 is hydrogen;

R^2 is hydrogen, alkyl, aralkyl, acyl, cycloalkyl, 25 hydroxy, thiol, halogen, amino, formyl, carboxy, cyano, nitro, alkylthio, haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, 30 alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group or

phenylalkyl;

R³

is

(1) alkyl or haloalkyl,

(2) cycloalkyl,

5 (3) phenyl optionally having substituent(s),

(4) aromatic heterocyclic group,

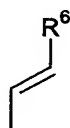
(5) a group derived from a benzene ring fused with a saturated or unsaturated 5 or 6 membered carbocyclic ring,

10 (6) a group derived from a benzene ring fused with a saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s), or

(7) a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring, wherein the groups of (2) to (7) may have one or more substituent(s), or

15

a group selected from the groups represented by the following formulas (II) and (III):



(II)



(III)

20

wherein R⁶ and R⁷ are each phenyl optionally having substituent(s) or an aromatic heterocyclic group, or R² and R³ in conjunction form a ring optionally containing heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);

25

R⁴ is alkoxycarbonyl,

alkylcarbonyl,

alkylsulfonyl,

alkylsulfinyl,

phenylsulfinyl,
 phenylsulfonyl,
 dialkylphosphinyl,
 dialkylphosphonyl,
 5 phenyl optionally having substituent(s),
 an aromatic heterocyclic group optionally having
 substituent(s),
 cyano or
 nitro; and
 10 R^5 is alkyl,
 phenylaminoalkyl,
 acyl,
 acylalkyl,
 aminocarbonyl,
 15 arylaminocarbonyl,
 a saturated or unsaturated 4 to 7 membered
 heterocyclic ring optionally having substituent(s),
 a saturated 3 to 7 membered carbocyclic ring having
 substituent(s),
 20 alkyl substituted by a saturated or unsaturated 4 to
 7 membered ring containing 1 or 2 nitrogen atom(s),
 which optionally has a substituent, or
 a group of the formula: $-(CR^aR^b)_nNR^{11}R^{12}$ wherein n is
 an integer of 1 to 4, R^a is hydrogen or alkyl, R^b is
 25 hydrogen or alkyl, R^{11} is hydrogen, alkyl,
 alkylsulfonyl, phenylsulfonyl, phenylalkylsulfonyl,
 alkylsulfinyl, phenylsulfinyl, phenylalkylsulfinyl,
 alkoxycarbonyl, phenoxycarbonyl, phenylalkoxycarbonyl,
 alkylcarbonyl, phenylcarbonyl or phenylalkylcarbonyl,
 30 and R^{12} is hydrogen or alkyl,
 provided that when R^0 , R^1 and R^2 are each hydrogen, R^4 is
 methoxycarbonyl and R^5 is methyl, then R^3 should not be phenyl,
 2-chlorophenyl, 3-nitrophenyl, 4-carboxyphenyl or 4-

methoxycarbonylphenyl, and when R⁵ is alkyl, then R⁴ is not alkoxycarbonyl, alkylsulfonyl, alkylsulfinyl, phenylsulfinyl, phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, cyano or nitro,

5 or an optically active form thereof, or a pharmaceutically acceptable salt thereof.

[13] The dihydropyrazolopyridine compound of the above-described [12], wherein

R⁴ is alkoxycarbonyl, alkylcarbonyl, alkylsulfonyl,
10 alkylsulfinyl, phenylsulfinyl, phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, phenyl optionally having substituent(s), an aromatic heterocyclic group having substituent(s), cyano or nitro, and
R⁵ is alkyl, phenylaminoalkyl, acyl, acylalkyl, aminocarbonyl,
15 arylaminocarbonyl, a saturated or unsaturated 4 to 7 membered heterocyclic ring optionally having substituent(s), a saturated 3 to 7 membered carbocyclic ring having substituent(s), alkyl substituted by a saturated or unsaturated 4 to 7 membered ring containing 1 or 2 nitrogen
20 atom(s), which optionally has a substituent, or a group of the formula: $-(CH_2)_nNR^{11}R^{12}$ wherein n is an integer of 1 to 4, R¹¹ is hydrogen, alkyl, alkylsulfonyl, phenylsulfonyl, phenylalkylsulfonyl, alkylsulfinyl, phenylsulfinyl, phenylalkylsulfinyl, alkoxycarbonyl, phenoxycarbonyl,
25 phenylalkoxycarbonyl, alkylcarbonyl, phenylcarbonyl or phenylalkylcarbonyl, and R¹² is hydrogen or alkyl, or an optically active form thereof, or a pharmaceutically acceptable salt thereof.

[14] The dihydropyrazolopyridine compound of the above-described [12] or [13], wherein R² is hydrogen or alkyl, or an
30 optically active form thereof, or a pharmaceutically acceptable salt thereof.

[15] The dihydropyrazolopyridine compound of the above-

described [12] or [13], wherein R^3 is phenyl optionally having 1 to 3 substituent(s), naphthyl, 2,1,3-benzoxadiazol-4-yl or 3,4-dihydro-2H-benzopyran-8-yl, or an optically active form thereof, or a pharmaceutically acceptable salt thereof.

5 [16] The dihydropyrazolopyridine compound of the above-described [12] or [13], wherein R^4 is alkoxycarbonyl having 2 to 5 carbon atoms, alkylcarbonyl having 2 to 5 carbon atoms, alkylsulfonyl having 1 to 4 carbon atoms, or alkylsulfinyl having 1 to 4 carbon atoms, or an optically active form
10 thereof, or a pharmaceutically acceptable salt thereof.

[17] The dihydropyrazolopyridine compound of the above-described [12] or [13], wherein R^5 is a group of the formula: $-(CH_2)_nNR^{11}R^{12}$ wherein n is an integer of 1 to 4, R^{11} is hydrogen, alkyl or alkoxycarbonyl and R^{12} is hydrogen or alkyl, or an
15 optically active form thereof, or a pharmaceutically acceptable salt thereof.

[18] The dihydropyrazolopyridine compound of the above-described [12] or [13], wherein R^0 is hydrogen or a group of the formula: $-COOR^8$ (wherein R^8 is alkyl, aryl optionally
20 having substituent(s) or aralkyl optionally having substituent(s)), or an optically active form thereof, or a pharmaceutically acceptable salt thereof.

[19] The dihydropyrazolopyridine compound of the above-described [12] or [13], which is selected from the group
25 consisting of

- (1002) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,
(1003) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,
30 (1011) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methylmorpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine,
(1014) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]-

pyridine,

(1023) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-(N,N-dimethylamino)cyclohexyl)-2H-pyrazolo[3,4-b]pyridine,

(1027) 6-(1-acetyl-1,2,3,6-tetrahydropyridin-4-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,

(1033) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-ethylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,

(1037) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,

(1038) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,

(1041) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-3-yl)-2H-pyrazolo[3,4-b]pyridine,

(1046) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(4-methylmorpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine,

(1048) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine,

(1051) 6-(1-acetylpiperidin-4-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,

(1052) 6-(1-benzoylpiperidin-4-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,

(1053) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methanesulfonylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,

(1059) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-oxocyclohexan-1-yl)-2H-pyrazolo[3,4-b]pyridine,

(1062) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(2-oxocyclohexan-1-yl)-2H-pyrazolo[3,4-b]pyridine,

(1063) 6-acetylmethyl-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,

(1073) 5-cyano-4,7-dihydro-4-(2,3-(methylenedioxy)phenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine,

- (1075) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-6-carboxylic acid phenylamide,
- (1078) 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(4-phenylpiperazin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine,
- 5 (1081) 6-acetyl-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,
- (1082) 6-acetyl-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,
- (1084) 4-(2-bromo-3-cyanophenyl)-5-(pyridin-2-yl)-4,7-dihydro-10 6-propyl-2H-pyrazolo[3,4-b]pyridine,
- (1086) 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(pyrrolidin-3-yl)-2H-pyrazolo[3,4-b]pyridine, and
- (1087) 4-(2,1,3-benzoxadiazol-4-yl)-5-(pyridin-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- 15 a tautomer thereof, an optically active form thereof, or a pharmaceutically acceptable salt thereof.
- [20] A medicament comprising a dihydropyrazolopyridine compound of the above-described [1] or [2], an optically active form thereof, a pharmaceutically acceptable salt 20 thereof or a hydrate thereof.
- [21] A medicament comprising a dihydropyrazolopyridine compound of the above-described [12] or [13], an optically active form thereof, or a pharmaceutically acceptable salt thereof.
- 25 [22] A pharmaceutical composition comprising a dihydropyrazolopyridine compound of the above-described [1] or [2], an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof, and a pharmaceutically acceptable additive.
- 30 [23] A pharmaceutical composition comprising a dihydropyrazolopyridine compound of the above-described [12] or [13], an optically active form thereof, or a pharmaceutically acceptable salt thereof, and a

- pharmaceutically acceptable additive.
- [24] A glycogen synthase kinase-3 beta inhibitor comprising a compound selected from the group consisting of a dihydropyrazolopyridine compound of the above-described [1] or [2], an optically active form thereof, a pharmaceutically acceptable salt thereof and a hydrate thereof.
- [25] A glycogen synthase kinase-3 beta inhibitor comprising a compound selected from the group consisting of a dihydropyrazolopyridine compound of the above-described [12] or [13], an optically active form thereof and a pharmaceutically acceptable salt thereof.
- [26] The medicament of the above-described [20] or [21], which is used for prevention and/or treatment of a disease caused by glycogen synthase kinase-3 beta hyperactivity.
- [27] The medicament of the above-described [20] or [21], which is used for prevention and/or treatment of a neurodegenerative disease.
- [28] The medicament of the above-described [27], wherein the disease is selected from the group consisting of Alzheimer's disease, ischemic cerebrovascular disorders, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, Parkinsonism dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease and manic-depressive psychosis.
- [29] The medicament of the above-described [20] or [21], which is used for prevention and/or treatment of diabetes and diabetic complications.
- [30] The medicament of the above-described [20] or [21], which is used as an immunopotentiator.
- [31] The medicament of the above-described [20] or [21], which

is used for prevention and/or treatment of alopecia, breast cancer, non-small cell lung carcinoma, thyroid cancer, T or B-cell leukemia or virus-induced tumors.

BRIEF DESCRIPTION OF THE DRAWINGS

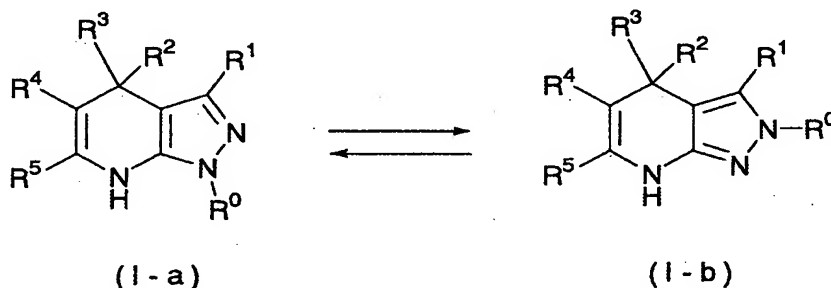
5 Fig. 1 shows the GSK-3 β -inhibitory activity of the compounds of Example 47 and Example 137.

Fig. 2 shows the effect of the compound of Example 66 on amyloid β -induced cytotoxicity.

10 Fig. 3 shows the GSK-3 β -inhibitory effect of the compound of Example 27 in a gerbil brain ischemia model.

DETAILED DESCRIPTION OF THE INVENTION

The formula (I) indicates the presence of tautomers represented by the following formulas (I-a) and (I-b), based on the positions of hydrogen atoms of the pyrazole ring. The present invention encompasses each isomer of the formulas (I-a) and (I-b), and a mixture of these isomers.



The compounds represented by the formula (I) in the present specification are described in detail in the following.

20 "Alkyl" means a linear or branched (hydro)carbon chain of 1 to 8 carbon atom(s), and includes methyl, ethyl, propyl, butyl, pentyl (i.e., amyl), hexyl, or a structural isomer thereof, such as isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-pentyl and the like, with a preference for alkyl having 1 to 4 carbon atom(s). The alkyl of R² is preferably alkyl having 1 to 4 carbon atoms. The alkyl of R⁵ is preferably alkyl having 2 to 8 carbon atoms.

The "alkyl having 2 to 8 carbon atoms" concretely includes ethyl, propyl, butyl, pentyl (i.e., amyl), hexyl, heptyl and octyl, or a structural isomer thereof, such as isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-
5 pentyl and the like. Alkyl having 2 to 4 carbon atoms is more preferable, and propyl is particularly preferable.

"Acyl" means C_2-C_{14} acyl, and includes "alkylcarbonyl" having 2 to 8 carbon atoms, such as acetyl, propionyl, butyryl, isobutyryl, valeryl, pivaloyl, hexanoyl, heptanoyl and the
10 like, at R^4 preferably having 2 to 5 carbon atoms, and aromatic acyl having 7 to 12 carbon atoms including " C_7-C_{12} arylcarbonyl" such as benzoyl, naphthoyl and the like and " C_7-C_{12} aralkylcarbonyl" such as benzylcarbonyl, 2-phenylethylcarbonyl, 3-phenylpropylcarbonyl, cinnamoyl, and the like, and the like.
15 The benzene and naphthalene rings may have 1 to 5 substituent(s) and substitution sites are not particularly limited.

"Acylalkyl" is acylalkyl consisting of the above C_1-C_8 alkyl and the above C_2-C_{14} acyl, and includes, for example,
20 acetylmethyl, propionylmethyl, butyrylmethyl, isobutyrylmethyl, valerylmethyl, pivaloylmethyl, 2-acetylethyl, 2-propionylethyl, 3-acetylpropyl and the like.

"Cycloalkyl" means a cyclic (hydro)carbon chain of 3 to 8 carbon atoms. Cycloalkyl concretely includes, for example,
25 cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like, with a preference for cycloalkyl having 3 to 6 carbon atoms. The cycloalkyl may have 1 to 5 substituent(s) and substitution sites are not particularly limited.

"Halogen" represents fluorine, chlorine, bromine or
30 iodine.

"Amino" is primary amino, secondary or tertiary amino having the above alkyl (e.g., C_1-C_8 alkyl), and includes, for example, amino, mono- or di- C_1-C_8 alkyl-substituted amino such

as methylamino, dimethylamino, ethylamino, diethylamino, propylamino, dipropylamino, butylamino, dibutylamino and the like, with a preference for tertiary amino containing alkyl having 1 to 4 carbon atom(s).

5 "Alkylthio" is a linear or branched alkylthio having 1 to 6 carbon atom(s), and includes, for example, methylthio, ethylthio, propylthio, butylthio, pentylthio (i.e., amylthio), hexylthio and structural isomers thereof, such as isopropylthio, isobutylthio, sec-butylthio, tert-butylthio, 10 isopentylthio, neopentylthio, tert-pentylthio and the like, with a preference for alkylthio having 1 to 3 carbon atom(s).

"Phenylthio" means phenylthio optionally having 1 to 5 substituent(s) on the phenyl and substitution sites are not particularly limited.

15 "Haloalkyl" is the above alkyl (e.g., C₁-C₈ alkyl) substituted by 1 to 5 halogen(s), and represents fluoromethyl, chloromethyl, difluoromethyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl and the like.

"Aminoalkyl" is the above-mentioned alkyl (e.g., C₁-C₈ 20 alkyl) having the above amino, preferably primary amino, and includes, for example, aminomethyl, methylaminomethyl, dimethylaminomethyl, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl, 2-methylaminoethyl, 2-dimethylaminoethyl, 2-ethylaminoethyl, 2-diethylaminoethyl and the like, with a preference for 25 aminoalkyl containing alkyl having 1 to 4 carbon atom(s), and aminoalkyl containing alkyl having 1 to 4 carbon atom(s) having tertiary amino.

"Acylamino" is acylamino having the above acyl (e.g., C₂-C₁₄ acyl), and represents, for example, acetylamino, 30 propionylamino, butyrylamino, valerylamino, pivaloylamino, benzoylamino, phenylacetylamino, phenylpropionylamino, phenylbutyrylamino and the like.

"Alkoxy" is alkoxy having the above alkyl (e.g., C₁-C₈

alkyl), and includes, for example, methoxy, ethoxy, propoxy, butoxy, pentyloxy (i.e., amyloxy), hexyloxy and structural isomers thereof, such as isopropoxy, isobutoxy, sec-butoxy, tert-butoxy, isopentyloxy, neopentyloxy, tert-pentyloxy and
5 the like, with a preference for alkoxy having 1 to 4 carbon atom(s).

"Cycloalkoxy" is (cyclo)alkoxy having the above cycloalkyl (e.g., C₃-C₈ cycloalkyl), and includes, for example, cyclopropoxy, cyclobutoxy, cyclopentyloxy, cyclohexyloxy and
10 the like, with a preference for cycloalkoxy having cycloalkyl having 3 to 6 carbon atoms.

"Phenoxy" means phenyloxy optionally having 1 to 5 substituent(s) on the phenyl and substitution sites are not particularly limited.

15 "Phenylalkoxy" is phenylalkoxy having the above alkoxy (e.g., C₁-C₈ alkoxy), and includes, for example, benzyloxy, 1-phenylethoxy, 2-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 1-methyl-1-phenylethoxy, 1-methyl-2-phenylethoxy, 1-phenylpropoxy, 2-phenylpropoxy, 1-methyl-1-phenylpropoxy, 1-
20 methyl-2-phenylpropoxy, 1-methyl-3-phenylpropoxy and the like, with a preference for phenylalkoxy containing alkoxy having 1 to 4 carbon atom(s).

The phenylalkoxy optionally has 1 to 5 substituent(s) on the phenyl and substitution sites are not particularly limited.

25 "Aminoalkoxy" is aminoalkoxy consisting of the above alkoxy (e.g., C₁-C₈ alkoxy) and amino, and includes, for example, aminomethoxy, methylaminomethoxy, dimethylaminomethoxy, 2-(dimethylamino)ethoxy, 3-(dimethylamino)propoxy, 4-(dimethylamino)butoxy and the like,
30 with a preference for aminoalkoxy consisting of tertiary amino containing alkyl having 1 to 4 carbon atom(s), and alkoxy having 1 to 4 carbon atom(s).

"Alkoxyalkyl" is alkoxyalkyl consisting of the above

alkoxy (e.g., C₁-C₈ alkoxy) and alkyl (e.g., C₁-C₈ alkyl), and includes, for example, methoxymethyl, ethoxymethyl, 2-methoxyethyl, propoxymethyl, isopropoxymethyl and the like, with a preference for alkoxyalkyl consisting of alkoxy having
5 1 to 4 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Phenoxyalkyl" is phenoxyalkyl containing of the above phenoxy and alkyl (e.g., C₁-C₈ alkyl), and includes, for example, phenoxymethyl, 2-phenoxyethyl, 3-phenoxypropyl and the like, with a preference for phenoxyalkyl containing alkyl
10 having 1 to 4 carbon atom(s). The phenoxyalkyl optionally has 1 to 5 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Dialkoxyalkyl" is dialkoxyalkyl consisting of the above alkyl and alkoxy, and includes, for example, dimethoxymethyl,
15 diethoxymethyl, 2,2-dimethoxyethyl, 2,2-diethoxyethyl and the like, with a preference for dialkoxyalkyl consisting of alkoxy having 1 to 4 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Hydroxyalkyl" is hydroxyalkyl having the above alkyl
20 (e.g., C₁-C₈ alkyl), and includes, for example, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl and the like, with a preference for hydroxyalkyl containing alkyl having 1 to 4 carbon atom(s).

"Alkoxy carbonyl" is alkoxy carbonyl having the above
25 alkoxy (e.g., C₁-C₈ alkoxy), and includes, for example, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl and structural isomers thereof, such as isopropoxycarbonyl, isobutoxycarbonyl, sec-butoxycarbonyl, tert-butoxycarbonyl,
30 isopentyloxycarbonyl, neopentyloxycarbonyl, tert-pentyloxycarbonyl and the like, with a preference for alkoxy carbonyl, in which the alkoxy moiety has 1 to 4 carbon atom(s). However, the alkoxy carbonyl of R⁴ is preferably

alkoxycarbonyl having 2 to 5 carbon atoms.

"Phenoxycarbonyl" is phenoxycarbonyl optionally having 1 to 5 substituent(s) on the phenyl and substitution sites are not particularly limited.

5 "Aminocarbonyl" is aminocarbonyl having the above amino (including mono- or di- C_1 - C_8 alkyl-substituted amino), and includes, for example, aminocarbonyl (i.e., carbamoyl), methylaminocarbonyl, dimethylaminocarbonyl, ethylaminocarbonyl, diethylaminocarbonyl, propylaminocarbonyl,
10 dipropylaminocarbonyl, phenylcarbamoyl, benzylcarbamoyl and the like, with a preference for tertiary-aminocarbonyl containing alkyl having 1 to 4 carbon atom(s).

"Alkylthiocarbonyl" is alkylthiocarbonyl having the above alkylthio (e.g., C_1 - C_6 alkylthio), and includes, for
15 example, methylthiocarbonyl, ethylthiocarbonyl, propylthiocarbonyl, butylthiocarbonyl and structural isomers thereof, such as isopropylthiocarbonyl, isobutylthiocarbonyl, sec-butylthiocarbonyl, tert-butylthiocarbonyl and the like, with a preference for alkylthiocarbonyl, in which the alkyl
20 moiety has 1 to 3 carbon atoms.

"Carboxyalkyl" is carboxyalkyl having the above alkyl (e.g., C_1 - C_8 alkyl), and includes, for example, carboxymethyl, carboxyethyl, carboxypropyl and the like, with a preference for carboxyalkyl containing alkyl having 1 to 4 carbon atom(s).

25 "Cycloalkoxyalkyl" is cycloalkoxyalkyl having the above cycloalkoxy and alkyl (e.g., cycloalkoxyalkyl consisting of the above C_3 - C_8 cycloalkoxy and C_1 - C_8 alkyl), and includes, for example, cyclopropoxymethyl, cyclopropoxyethyl, cyclobutoxymethyl, cyclopentyloxymethyl, cyclohexyloxymethyl
30 and the like, with a preference for cycloalkoxyalkyl consisting of cycloalkoxy having 3 to 6 carbon atoms and alkyl having 1 to 4 carbon atom(s). The cycloalkoxyalkyl optionally has 1 to 3 substituent(s) on the cycloalkyl and substitution

sites are not particularly limited.

"Alkylsulfinyl" is alkylsulfinyl having the above alkyl (e.g., C₁-C₈ alkyl), and includes, for example, methylsulfinyl, ethylsulfinyl, propylsulfinyl, isopropylsulfinyl and the like, 5 with a preference for alkylsulfinyl containing alkyl having 1 to 5, preferably 1 to 4 carbon atom(s). The alkylsulfinyl of R⁴ is preferably alkylsulfinyl having 1 to 4 carbon atoms.

"Phenylsulfinyl" means phenylsulfinyl optionally having 1 to 5 substituent(s) on the phenyl and substitution sites are 10 not particularly limited.

"Alkylsulfonyl" is alkylsulfonyl having the above alkyl (e.g., C₁-C₈ alkyl), and includes, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl and the like, with a preference for alkylsulfonyl containing alkyl having 1 15 to 5, preferably 1 to 4 carbon atom(s). The alkylsulfonyl of R⁴ is preferably alkylsulfonyl having 1 to 4 carbon atoms.

"Phenylsulfonyl" means phenylsulfonyl optionally having 1 to 5 substituent(s) on the phenyl and substitution sites are not particularly limited.

20 "Mercaptoalkyl" is mercaptoalkyl having the above alkyl (e.g., C₁-C₈ alkyl), and includes, for example, mercaptomethyl, mercaptoethyl, mercaptopropyl and the like, with a preference for mercaptoalkyl containing alkyl having 1 to 4 carbon atom(s).

25 "Alkylthioalkyl" is alkylthioalkyl having the above alkylthio and alkyl (e.g., alkylthioalkyl consisting of the above C₁-C₆ alkylthio and C₁-C₈ alkyl), and includes, for example, methylthiomethyl, methylthioethyl, methylthiopropyl, ethylthiomethyl, ethylthioethyl, ethylthiopropyl and the like, 30 with a preference for alkylthioalkyl consisting of alkylthio having 1 to 3 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Aryl" is aryl having 6 to 14 carbon atoms, and includes,

for example, phenyl, 1-naphthyl, 2-naphthyl, 1-anthryl, 2-anthryl and the like. They may have 1 to 5 substituent(s) and substitution sites are not particularly limited.

"Aralkyl" is aralkyl wherein the above alkyl (e.g., C₁-C₈ alkyl) is substituted by the above aryl (e.g., C₆-C₁₄ aryl), and includes benzyl, 2-phenylethyl, 3-phenylpropyl, 1-naphthylmethyl, 2-naphthylmethyl and the like. These may have 1 to 5 substituent(s) on the aryl moiety and substitution sites are not particularly limited.

10 "Acyloxyacetyl" is acyloxyacetyl having the above acyl (e.g., C₂-C₁₄ acyl), and includes, for example, acetyloxyacetyl, propionyloxyacetyl, butyryloxyacetyl, benzoyloxyacetyl and the like.

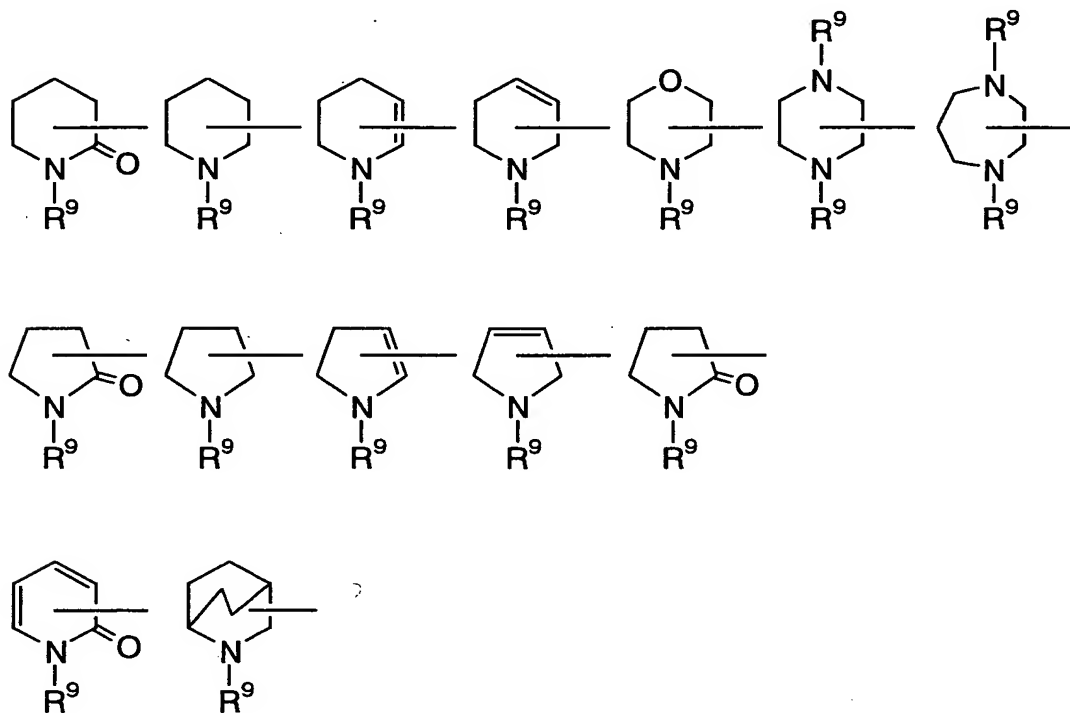
"Acyloxyalkyl" is acyloxyalkyl having the above acyl (e.g., C₂-C₁₄ acyl) and alkyl (e.g., C₁-C₈ alkyl), and includes, for example, acetyloxymethyl, propionyloxymethyl, butyryloxymethyl, benzoyloxymethyl, 2-acetyloxyethyl, 2-propionyloxyethyl, 2-butyryloxyethyl, 2-benzoyloxyethyl and the like.

20 The substituent of the "phenyl optionally having substituent(s)" is exemplified by those mentioned for the "substituent" below, wherein the number of the substituent is generally 1 to 5, preferably 1 to 3, more preferably 3. Phenyl having 1 or 2 substituent(s) is particularly preferable and substitution sites are not particularly limited.

"Aromatic heterocyclic group" is, for example, a 5- or 6-membered aromatic heterocyclic group optionally containing 1 to 3 heteroatom(s) selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom, and includes, for example, thiophenyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, oxadiazolyl (e.g., 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, etc.), and the like. The

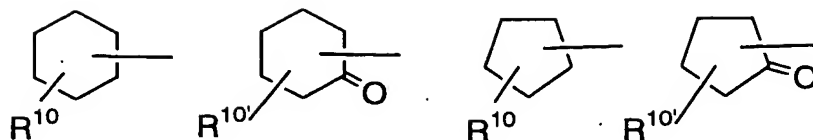
aromatic heterocyclic group may have 1 to 6 substituent(s) and substitution sites are not particularly limited.

"Saturated or unsaturated 4 to 7 membered heterocyclic ring optionally having substituent(s)" includes the following groups and the like.



10 wherein R^9 is each independently hydrogen, alkyl, acyl, aralkyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, phenylalkyl, alkoxyalkyl, phenoxyalkyl, guan-
 15 yl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, alkoxy carbonyl, phenoxy carbonyl, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, aryl optionally having substituent(s), aromatic heterocyclic group optionally having substituent(s), or phenylalkyl optionally having
 20 substituent(s).

"Saturated 3 to 7 membered carbocyclic ring having substituent(s)" includes the following groups and the like.



wherein R^{10} is alkyl, acyl, aralkyl, cycloalkyl, formyl,
 5 haloalkyl, aminoalkyl, alkoxyalkyl, phenylalkyl,
 phenoxyalkyl, amino, hydroxyalkyl, aminocarbonyl,
 alkylthiocarbonyl, carboxyalkyl, alkylsulfinyl,
 alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
 alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, aryl
 10 optionally having substituent(s), aromatic
 heterocyclic group optionally having substituent(s),
 or phenylalkyl optionally having substituent(s),
 and $R^{10'}$ is hydrogen, alkyl, acyl, aralkyl,
 cycloalkyl, formyl, haloalkyl, aminoalkyl,
 15 alkoxyalkyl, phenylalkyl, phenoxyalkyl, amino,
 hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl,
 carboxyalkyl, alkylsulfinyl, alkylsulfonyl,
 phenylsulfonyl, mercaptoalkyl, alkylthioalkyl,
 acyloxyacetyl, acyloxyalkyl, aryl optionally having
 20 substituent(s), aromatic heterocyclic group
 optionally having substituent(s), or phenylalkyl
 optionally having substituent(s).

The substituent of the "aromatic heterocyclic group
 optionally having substituent(s)" is exemplified by those
 25 mentioned for the "substituent" below, wherein the number of
 the substituent is generally 1 to 6, preferably 1 to 5, more
 preferably 3, and substitution sites are not particularly
 limited.

"Phenylalkyl" is phenylalkyl having the above alkyl
 30 (e.g., phenylalkyl consisting of phenyl and the above C_1-C_8
 alkyl), and includes, for example, benzyl, 2-phenylethyl, 3-

phenylpropyl, 4-phenylbutyl, 1-phenylethyl, 1-methyl-2-phenylethyl, 1-phenylpropyl, 2-phenylpropyl, 1-methyl-1-phenylpropyl, 1-methyl-2-phenylpropyl, 1-methyl-3-phenylpropyl and the like, with a preference for phenylalkyl consisting of
5 phenyl and alkyl having 1 to 4 carbon atom(s).

The kind and the number of the substituent of the "phenylalkyl optionally having substituent(s)" are the same as those for the above-mentioned "aromatic heterocyclic group" and substitution sites are not particularly limited.

10 "Alkoxy carbonylalkyl" is alkoxy carbonylalkyl having the above alkoxy carbonyl and alkyl, and includes, for example, methoxycarbonylmethyl, ethoxycarbonylmethyl, ethoxycarbonylmethyl, 2-ethoxycarbonylethyl, 3-ethoxycarbonylpropyl and the like.

15 "Alkoxy carbonylethenyl" is alkoxy carbonylethenyl having the above alkoxy carbonyl, and includes, for example, 2-methoxycarbonylethenyl, 2-ethoxycarbonylethenyl, 2-butoxycarbonylethenyl, 2-tert-butoxycarbonylethenyl and the like.

20 "Dialkylphosphinyl" is dialkylphosphinyl having the above alkyl (e.g., C₁-C₈ alkyl), and includes, for example, dimethylphosphinyl, diethylphosphinyl, dipropylphosphinyl and the like, with a preference for dialkylphosphinyl containing alkyl having 1 to 4 carbon atom(s).

25 "Dialkylphosphonyl" is dialkylphosphonyl having the above alkyl (e.g., C₁-C₈ alkyl), and includes, for example, dimethylphosphonyl, diethylphosphonyl, dipropylphosphonyl and the like, with a preference for dialkylphosphonyl containing alkyl having 1 to 4 carbon atom(s).

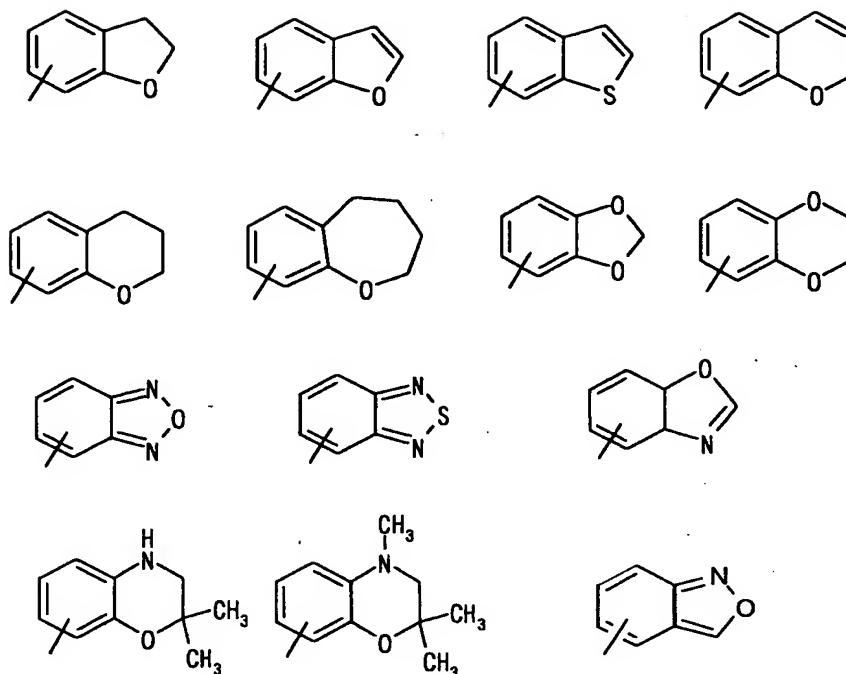
30 In the present specification, "substituent" includes alkyl, acyl, cycloalkyl, phenyl, aromatic heterocyclic group, phenylalkyl, hydroxy, carboxy, thiol, halogen, amino, formyl, carbamoyl, cyano, nitro, alkylthio, haloalkyl, aminoalkyl,

acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl, alkylsulfinyl, aminocarbonyl, alkylthiocarbonyl and the like.

5 "Ring optionally containing heteroatom(s)" is a 5 or 6 membered carbocyclic ring optionally containing 1 to 3 heteroatom(s) selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom, with particular preference given to a ring containing sulfur atom. The ring may be
10 substituted by one or more of the above substituents or oxo groups. The substitution site is not particularly limited. This ring is formed by R^2 and R^3 in the formula (I) together with the attached carbon atom. By forming this ring, a spiro ring is formed in the compound of the formula (I). The above
15 ring can be fused with a benzene ring optionally having substituent(s) and substitution sites are not particularly limited. Such a ring includes, for example, 2,3-dihydrobenzo[b]thiophene, 2,3-dihydrobenzo[b]thiophen-1-oxide and the like.

20 "A group derived from a benzene ring fused with a saturated or unsaturated 5 or 6 membered carbocyclic ring" represents a group derived from naphthalene, 1,2-dihydronaphthalene, 1,2,3,4-tetrahydronaphthalene, indan and the like, with preference given to naphthalene (namely
25 naphthyl) and particular preference given to 1-naphthyl. Of these, naphthyl such as naphthalen-1-yl and the like, and indanyl such as indan-4-yl and the like are preferable. The group may have 1 to 4 substituent(s) and substitution sites are not particularly limited.

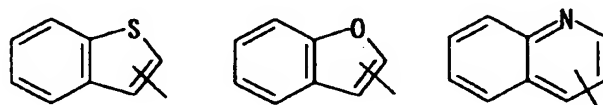
30 "A group derived from a benzene ring fused with a saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s)" includes the following groups and the like.



Of these, 2,1,3-benzoxadiazole, dihydrobenzo[b]furan, methylenedioxyphenyl and 3,4-dihydro-2H-benzopyrane are preferable, and 2,1,3-benzoxadiazol-4-yl, 2,3-dihydrobenzo-
 5 [b]furan-7-yl, 2,3-(methylenedioxy)phenyl and 3,4-dihydro-2H-benzopyran-8-yl are particularly preferable. The group may have 1 to 3 substituent(s) and substitution sites are not particularly limited.

Of these, 2,1,3-benzoxadiazole and 3,4-dihydro-2H-
 10 benzopyrane are preferable, and 2,1,3-benzoxadiazol-4-yl and 3,4-dihydro-2H-benzopyran-8-yl are particularly preferable.

"A group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring" includes the following
 15 groups and the like.



The group may have 1 to 5 substituent(s) and

substitution sites are not particularly limited.

"Alkylcarbonylalkyl" is, for example, C₁-C₄ alkyl-carbonyl-C₁-C₄ alkyl, and includes, for example, methylcarbonylmethyl, ethylcarbonylmethyl, propylcarbonylmethyl, butylcarbonylmethyl and the like.

"Arylaminoalkyl" is C₆-C₁₀ aryl-aminoalkyl, and includes, for example, phenylaminoalkyl, naphthylaminoalkyl and the like. The arylaminoalkyl optionally has 1 to 3 substituent(s) on the aryl and substitution sites are not particularly limited.

"Aralkylaminoalkyl" is C₇-C₁₄ aralkyl-aminoalkyl, and includes, for example, benzylaminoalkyl and the like. The aralkylaminoalkyl optionally has 1 to 3 substituent(s) on the aryl and substitution sites are not particularly limited.

"Alkyl substituted by a saturated or unsaturated 4 to 7 membered ring containing 1 or 2 nitrogen atom(s), which optionally has a substituent" means C₁-C₈ alkyl substituted by "a saturated or unsaturated 4 to 7 membered ring containing 1 or 2 nitrogen atom(s)", such as pyrrole, pyrrolidine, pyrazole, pyridine, piperidine, piperazine, homopiperazine or morpholine and the like, which optionally has a substituent such as C₁-C₄ alkyl, C₆-C₁₀ aryl such as phenyl, naphthyl and the like, and includes, for example, (4-phenylpiperazine-1-yl)methyl, 2-(4-phenylpiperazine-1-yl)ethyl, 3-(4-phenylpiperazine-1-yl)propyl, (4-(naphthalen-1-yl)piperazine-1-yl)methyl, 2-(4-(naphthalen-1-yl)piperazine-1-yl)ethyl, (4-methylhomopiperazine-1-yl)methyl and the like.

"Phenylaminoalkyl" is phenylamino-C₁-C₄ alkyl, and includes, for example, phenylaminomethyl, 2-phenylaminoethyl, 3-phenylaminopropyl, 4-phenylaminobutyl and the like. The phenylaminoalkyl optionally has 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Phenylalkylcarbonyl" is phenyl-C₁-C₄ alkyl-carbonyl, and

includes, for example, benzylcarbonyl, 2-phenylethylcarbonyl, 3-phenylpropylcarbonyl, 4-phenylbutylcarbonyl and the like. The phenylalkylcarbonyl optionally has 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly
5 limited.

"Alkyl" in the R^{11} is C_1 - C_4 alkyl, and includes, for examples, methyl, ethyl, propyl, isopropyl, butyl, iso-butyl, tert-butyl and the like.

"Alkylsulfonyl" in the R^{11} is C_1 - C_4 alkyl-sulfonyl, and
10 includes, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like.

"Phenylsulfonyl" in the R^{11} is phenylsulfonyl optionally having 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

15 "Phenylalkylsulfonyl" in the R^{11} is phenyl- C_1 - C_4 alkyl-sulfonyl, and includes, for example, benzylsulfonyl, 2-phenylethylsulfonyl, 3-phenylpropylsulfonyl, 4-phenylbutylsulfonyl and the like. The phenylalkylsulfonyl optionally has 1 to 3 substituent(s) on the phenyl and
20 substitution sites are not particularly limited.

"Alkylsulfinyl" in the R^{11} is C_1 - C_4 alkyl-sulfinyl, and includes, for example, methylsulfinyl, ethylsulfinyl, propylsulfinyl and the like.

"Phenylsulfinyl" in the R^{11} is phenylsulfinyl optionally
25 having 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Phenylalkylsulfinyl" in the R^{11} is phenyl- C_1 - C_4 alkyl-sulfinyl, and includes, for example, benzylsulfinyl, 2-phenylethylsulfinyl, 3-phenylpropylsulfinyl, 4-
30 phenylbutylsulfinyl and the like. The phenylalkylsulfinyl optionally has 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Alkoxy carbonyl" in the R^{11} is C_1 - C_4 alkoxy-carbonyl, and

includes, for example, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, tert-butoxycarbonyl and the like.

"Phenylalkoxycarbonyl" in the R^{11} is phenyl- C_1 - C_4 alkoxy-carbonyl, and includes, for example, benzyloxycarbonyl, 2-phenylethoxycarbonyl, 3-phenylpropoxycarbonyl, 4-phenylbutoxycarbonyl and the like. The phenylalkoxycarbonyl optionally has 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Alkylcarbonyl" in the R^{11} is C_1 - C_4 alkyl-carbonyl and includes, for example, acetyl, propionyl, butylcarbonyl and the like.

"Phenylcarbonyl" in the R^{11} is phenylcarbonyl optionally having 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Phenylalkylcarbonyl" in the R^{11} is phenyl- C_1 - C_4 alkyl-carbonyl, and includes, for example, benzylcarbonyl, 2-phenylethylcarbonyl, 3-phenylpropylcarbonyl, 4-phenylbutylcarbonyl and the like. The phenylalkylcarbonyl optionally has 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Phenoxycarbonyl" in the R^{11} means phenoxycarbonyl optionally having 1 to 3 substituent(s) on the phenyl and substitution sites are not particularly limited.

"Alkyl" in the R^{12} is C_1 - C_4 alkyl, and includes, for examples, methyl, ethyl, propyl, iso-propyl, butyl, iso-butyl, tert-butyl and the like.

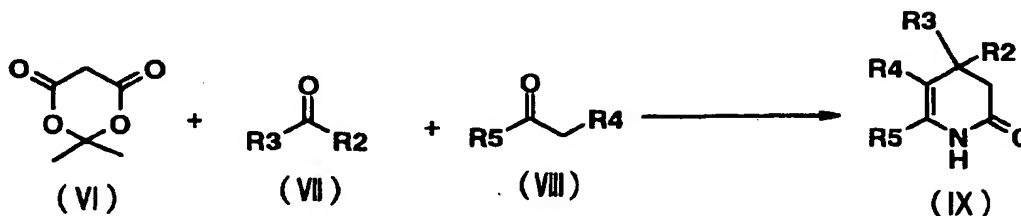
The "5 or 6-membered ring optionally containing heteroatom(s)" is a 5 or 6 membered carbocyclic ring optionally containing 1 to 3 heteroatom(s) consisting of nitrogen atom, oxygen atom and sulfur atom. Examples thereof include furan, thiophene, pyrrole, oxazole, isoxazole, thiazole, isothiazole, imidazole, pyrazole, furazan, pyran, pyridine, pyridazine, pyrimidine, pyrazine, pyrroline,

pyrrolidine, imidazoline and imidazolidine. Of these, furan, thiophene, pyrrole, oxazole, isoxazole, thiazole, isothiazole, furazan and pyridine are preferable.

The compounds represented by the formula (I) of the present invention can be converted to acid addition salts with pharmaceutically acceptable acids and such acid addition salts are also encompassed in the present invention. Such acid addition salts include, for example, salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and salts with organic acids such as formic acid, acetic acid, trifluoroacetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, citric acid, tartaric acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, glutamic acid and the like. Furthermore, the compounds of the present invention can form hydrates, solvates with ethanol and the like, and crystal polymorphs. When an asymmetric carbon atom exists, optical isomers and racemates thereof can be present, and all of these are encompassed in the present invention.

Of the compounds (I) of the present invention, a compound wherein R^0 is hydrogen can be synthesized as shown in the following according to the method described in J. Chem. Soc., Perkin Trans. 1, 947 (1996) and the like.

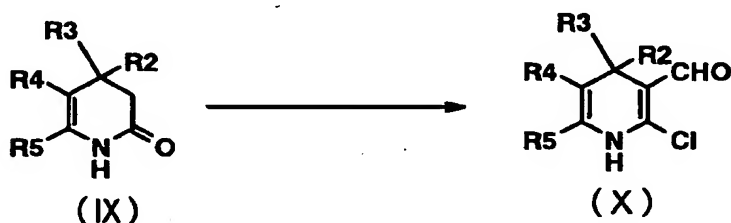
First Production Method



wherein R^2 , R^3 , R^4 and R^5 are as defined above.

Meldrum's acid of the formula (VI) and a carbonyl

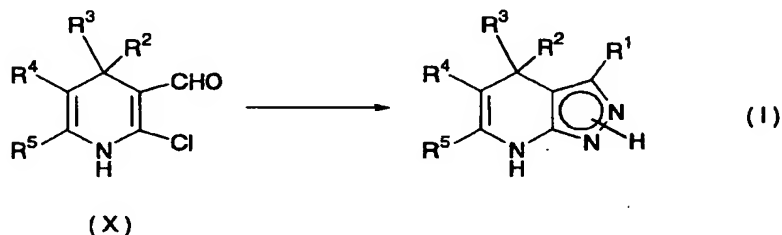
derivative of the formula (VII) are reacted with a carbonyl derivative of the formula (VIII), if desired, in the presence of ammonium acetate, to give an amide derivative of the formula (IX). The reaction is carried out in the presence of a
 5 carboxylic acid solvent inert to the reaction. As the solvent, formic acid, acetic acid, propionic acid, butyric acid, valeric acid and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.



10

wherein R², R³, R⁴ and R⁵ are as defined above.

The obtained amide derivative of the formula (IX) is reacted in the presence of dimethylformamide and phosphorus oxychloride to give a formyl derivative of the formula (X).
 15 The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide and the like are generally used. The reaction is
 20 carried out at any temperature, for example, from 0°C to 200°C, preferably from 0°C to 100°C, more preferably from 0°C to 60°C or 60°C to 100°C.



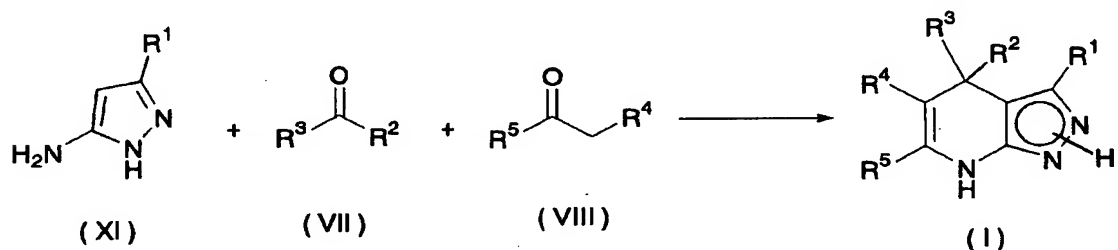
wherein R¹ (e.g., hydrogen), R², R³, R⁴ and R⁵ are as defined

above.

The compound (I) of the present invention can be produced by reacting the obtained formyl derivative of the formula (X) in the presence of hydrazine. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide, pyridine, alcohol and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

The carbonyl derivative of the formula (VII), which is a starting material, can be synthesized according to the methods described in J. Org. Chem., 46, 783 (1981), Eur. J. Med. Chem., 31, 3 (1996) and Tetrahedron Lett., 24, 5023 (1983). The carbonyl derivative of the formula (VIII) can be synthesized according to the method described in Synthesis, 290 (1993).

Second Production Method



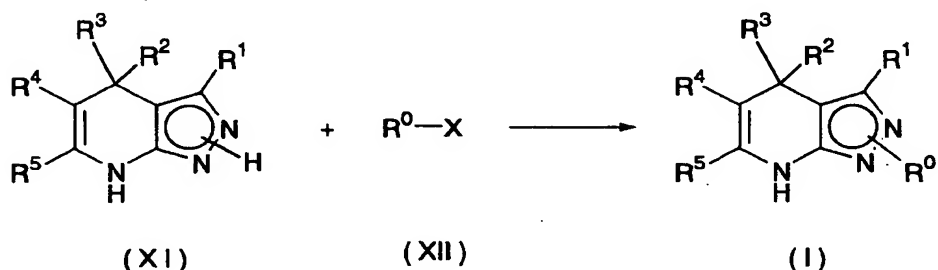
wherein R¹, R², R³, R⁴ and R⁵ are as defined above.

The compounds (I) of the present invention can be produced by reacting aminopyrazole of the formula (XI) and a carbonyl derivative of the formula (VII) with a carbonyl derivative of the formula (VIII). The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide, alcohol and the like

are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

Of the compounds (I) of the present invention, a compound wherein R⁰ is a substituent other than hydrogen can be synthesized as follows.

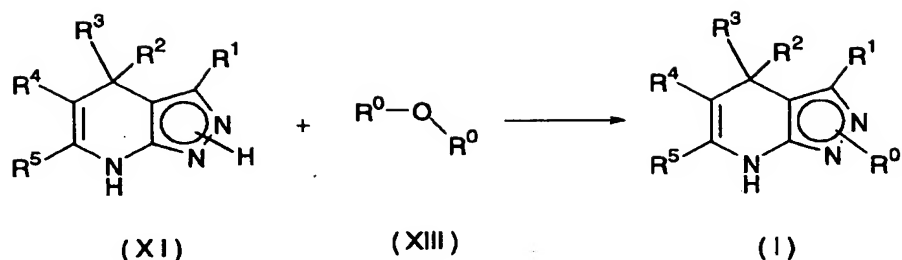
Third Production Method



wherein R⁰, R¹, R², R³, R⁴ and R⁵ are as defined above, and X represents halogen, provided that R⁰ is not hydrogen.

The compounds (I) of the present invention can be produced by reacting a dihydropyrazolopyridine derivative of the formula (XI) with halide of the formula (XII) in the presence of a base. Suitable base includes, for example, triethylamine, diisopropylethylamine, 4-dimethylaminopyridine and the like. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, one without hydroxy group is generally used, such as tetrahydrofuran, ethyl acetate, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethylimidazolidinone and the like. The reaction is carried out at any temperature, for example, from -10°C to 200°C, preferably from 0°C to 100°C.

Fourth Production Method



wherein R⁰, R¹, R², R³, R⁴ and R⁵ are as defined above, provided that R⁰ is not hydrogen.

The compounds (I) of the present invention can be produced by reacting a dihydropyrazolopyridine derivative of the formula (XI) with anhydride of the formula (XIII) such as acetic anhydride or the like in the presence of a base. Suitable base includes, for example, triethylamine, pyridine, 4-dimethylaminopyridine and the like. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, one without hydroxy group is generally used, such as tetrahydrofuran, ethyl acetate, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethylimidazolidinone, pyridine and the like. The reaction is carried out at any temperature, for example, from -10°C to 200°C, preferably from 0°C to 100°C.

Those skilled in the art should understand that the above production methods can be modified corresponding to the desired compounds.

The compound (I) of the present invention thus produced can be isolated and purified as a free compound or a salt thereof. Isolation and purification is carried out by a conventional chemical process such as extraction, concentration, evaporation, crystallization, filtration, recrystallization, various kinds of chromatography and the like. When the purified product thus obtained is a racemate, a desired optically active compound can be separated by, for example, fractional recrystallization with optically active

acid, or passing through a column packed with optically active carrier. The present invention also encompasses optically active compounds.

The compounds of the present invention obtained by the
5 above methods have a weak inhibitory activity on kinases other than GSK-3 β such as CaM kinase II, MAP kinase, Casein kinase, PKA, PKC and ROCK, but have a strong inhibitory activity on GSK-3 β . Therefore, the compounds of the present invention have a GSK-3 β -selective inhibitory activity and can be medicaments
10 with small side-effect for diabetes, diabetic complications, neurodegenerative diseases (Alzheimer's disease, ischemic cerebrovascular disorders, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism,
15 postencephalitic Parkinsonism, boxer's encephalopathy, Parkinsonism dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease, manic-depressive psychosis and the like), alopecia, breast cancer,
20 non-small cell lung carcinoma, thyroid cancer, T or B-cell leukemia, and several virus-induced tumors. In addition, the compounds of the present invention are useful as immunopotentiators.

Formulations comprising the compounds of the present
25 invention or salts thereof as an active ingredient are prepared using carriers, excipients and other additives conventionally used for formulation. The carrier and excipient for formulation may be a solid or liquid, and include, for example, lactose, magnesium stearate, starch such
30 as corn starch and the like, talc, gelatin, agar, pectin, gum Arabic, olive oil, sesame oil, cacao butter, ethylene glycol and other conventionally used substances. Administration may be oral administration of tablet, pill, capsule, granule,

powder, solution and the like, or parenteral administration by injection (intravenous injection, intramuscular injection and the like), suppository, transdermal agent and the like. While the dose is appropriately determined on each case in
5 consideration of symptom, age and sex of the administration subject, and the like, it is generally 1 - 1,000 mg, preferably 50 - 200 mg per day for an adult person, which is orally administered once to several times a day, or 1 - 500 mg per day for an adult person, which is intravenously
10 administered once to several times a day, or continuously administered intravenously for 1 to 24 hours a day.

As solid compositions for oral administration according to the present invention, tablet, powder, granule and the like are used. In such a solid composition, one or more active
15 substances are mixed with at least one inert diluent, such as lactose, mannitol, glucose, hydroxypropylcellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone, metasilicic acid and magnesium aluminate. The composition may contain, according to a conventional method, inert additives
20 other than diluent, for example, a lubricant such as magnesium stearate, a disintegrator such as cellulose and calcium glycolate, a stabilizer such as lactose and a solubilizer such as glutamic acid and aspartic acid. Tablet and pill may be coated with a gastric or enteric coating film of, for example,
25 sucrose, gelatin, hydroxypropylcellulose and the like. Liquid compositions for oral administration include pharmaceutically acceptable emulsion, solution, suspension, syrup, elixir and the like, and contain an inert diluent generally used, such as purified water and ethanol. This composition may contain an
30 adjuvant such as wetting agent and suspending agent, a sweetener, a flavor, an aromatic and an antiseptic, in addition to the inert diluent. Injections for parenteral administration contain sterile aqueous or non-aqueous solution,

suspension and emulsion. The aqueous solution and suspension include, for example, propylene glycol, polyethylene glycol, vegetable oil such as olive oil, alcohols such as ethanol, polysorbate 80 and the like. Such a composition may contain
5 adjuvants such as antiseptic, wetting agent, emulsifier, dispersant, stabilizer and solubilizer. These are sterilized by, for example, filtration through a bacteria-retaining filter, addition of an antimicrobial agent, irradiation of ultraviolet ray and the like. Alternatively, a sterile solid
10 composition may be prepared and used upon dissolution in sterile water or sterile solvent for injection prior to use.

Examples

The present invention is described in detail in the following, based on Examples, Formulation Examples and
15 Experimental Examples. The scope of the present invention is not limited to these examples.

Example 1

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 A solution of 2-chlorobenzaldehyde (1.7 g), 3-aminopyrazole (1.0 g) and ethyl acetoacetate (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature and the solvent was evaporated under reduced pressure to give an oil.
25 The oil was purified by silica gel column chromatography (eluent: hexane- ethyl acetate (8:2)) to give the title compound (850 mg) as colorless crystals.

Melting Point (MP): 217-221°C.

Anal. Calcd. for: C₁₆H₁₆N₃O₂Cl: C, 60.47; H, 5.08; N, 13.22.

30 Found: C, 60.15; H, 5.07; N, 13.53.

MS (EI): 317 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.00 (3H, t, J=6.8Hz), 2.25 (3H, s), 3.72-3.82 (2H, m), 5.57 (1H, s), 7.07-7.12 (2H, m),

7.18 (1H, d, J=7.3Hz), 7.26 (1H, s), 7.34 (1H, d, J=7.9Hz),
9.53 (1H, br. s), 11.98 (1H, br. s).

IR (KBr): ν =3393, 3267, 1670, 1589, 1518, 1278, 1217 cm^{-1} .

Example 2

5 Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-methyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 1.

10 MP: 196-200°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O} \cdot 1/5 \text{H}_2\text{O}$: C, 64.42; H, 6.17; N, 13.26.

Found: C, 64.08; H, 6.05; N, 13.68.

MS (EI): 313 (M^+).

^1H -NMR (400MHz, DMSO-d_6) δ (ppm): 1.00 (3H, t, J=6.8Hz), 2.81 (3H, s),
15 3.72 (3H, s), 3.87 (2H, q, J=6.8Hz), 5.54 (1H, s), 6.80 (1H, dd, J=7.3Hz
and 7.4Hz), 6.90 (1H, d, J=7.8Hz), 7.04 (1H, d, J=7.4Hz), 7.13-
7.15 (2H, m), 9.99 (1H, br. s), 11.98 (1H, br. s).

IR (KBr): ν =3362, 3267, 3204, 3090, 1662, 1589, 1516, 1275, 1097 cm^{-1} .

Example 3

20 Ethyl 4,7-dihydro-6-methyl-4-(2-trifluoromethylphenyl)-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 1.

25 MP: 259-262°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2 \cdot 1/5 \text{H}_2\text{O}$: C, 57.53; H, 4.66; N, 11.84.

Found: C, 57.56; H, 4.68; N, 11.86.

MS (EI): 352 ($\text{M}^+ + 1$).

^1H -NMR (400MHz, DMSO-d_6) δ (ppm): 0.74 (3H, t, J=6.9Hz), 2.40 (3H, s),
30 3.68-3.81 (2H, m), 5.42 (1H, s), 7.00 (1H, s), 7.28 (1H, dd, J=7.3Hz and
7.4Hz), 7.33 (1H, d, J=7.2Hz), 7.51 (1H, dd, J=7.3Hz and 7.4Hz),
7.60 (1H, d, J=7.8Hz), 9.58 (1H, br. s), 12.00 (1H, br. s).

IR (KBr): ν =3277, 3209, 3094, 1668, 1593, 1514, 1313, 1213, 1153, 1097,

765cm⁻¹.

Example 4

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl acetoacetate in the same manner as in Example 1.

MP:235°C.

Anal. Calcd. for: C₁₅H₁₄ClN₃O₂ 2/5 H₂O: C, 57.94; H, 4.80; N, 13.51.

10 Found: C, 58.03; H, 4.55; N, 13.43.

MS(EI): 303 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.40 (3H, s), 3.34 (3H, s), 5.55 (1H, s), 7.09-7.11 (2H, m), 7.18 (1H, dd, J=7.3Hz and 7.4Hz), 7.29 (1H, s), 7.34 (1H, d, J=7.3Hz), 9.57 (1H, br.s), 12.00 (1H, br.s).

15 Example 5

t-Butyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and t-butyl acetoacetate
20 in the same manner as in Example 1.

MP:207°C.

Anal. Calcd. for: C₁₈H₂₀ClN₃O₂: C, 62.52; H, 5.83; N, 12.15.

Found: C, 62.51; H, 5.79; N, 12.17.

MS(EI): 345 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.07 (9H, s), 2.36 (3H, s), 5.50 (1H, s), 7.11-7.15 (2H, m), 7.20 (1H, d, J=7.3Hz), 7.25 (1H, s), 7.37 (1H, d, J=7.3Hz), 9.35 (1H, br.s), 11.93 (1H, br.s).

Example 6

Isopropyl 4-(2-fluorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and isopropyl acetoacetate in the same manner as in Example 1.

MP:218-220°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.66(3H, d, J=6.3Hz),
1.02(3H, d, J=6.3Hz), 2.37(3H, s), 4.66(1H, q, J=6.3Hz), 5.40(1H, s),
7.01-7.14(4H, m), 7.19(1H, s), 9.46(1H, br.s), 11.97(1H, br.s).

5 **Example 7**

Benzyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-
chlorobenzaldehyde, 3-aminopyrazole and benzyl acetoacetate in
10 the same manner as in Example 1.

MP:234°C.

Anal. Calcd. for: C₂₁H₁₈ClN₃O₂: C, 66.40; H, 4.78; N, 11.06.

Found: C, 66.16; H, 4.86; N, 10.92.

MS(EI): 379 (M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.43(3H, s), 4.81(1H, d, J=12.6Hz),
4.92(1H, d, J=12.6Hz), 5.62(1H, s), 6.86-6.88(2H, m), 7.13-
7.18(6H, m), 7.31-7.34(2H, m), 9.65(1H, br.s), 12.01(1H, br.s).

Example 8

4-(2-Chlorophenyl)-5-dimethylaminocarbonyl-4,7-dihydro-6-
20 methyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-
chlorobenzaldehyde, 3-aminopyrazole and N,N-dimethylacetamide
in the same manner as in Example 1.

MP:229°C.

25 Anal. Calcd. for: C₁₆H₁₇ClN₄O 1/2 H₂O: C, 58.99; H, 5.57; N, 17.20.

Found: C, 58.90; H, 5.46; N, 16.84.

MS(EI): 316 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.77(3H, s), 2.72(6H, s),
5.39(1H, s), 7.10-7.22(4H, m), 7.30(1H, d, J=7.3Hz), 8.40(1H, br.s),
30 11.83(1H, br.s).

Example 9

4-(2-Chlorophenyl)-5-hydrazinocarbonyl-4,7-dihydro-6-methyl-
2H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2-chlorophenyl)-4,7-dihydro-5-dimethylaminocarbonyl-6-methyl-2H-pyrazolo[3,4-b]pyridine (200 mg) in acetonitrile (200 mL) was added hydrazine (200 mg) and the mixture was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration and washed with ethyl acetate to give the title compound as colorless crystals (150 mg).

MP:220°C.

10 Anal. Calcd. for: $C_{14}H_{14}ClN_5O$ 3/10 H_2O : C, 54.39; H, 4.76; N, 22.65.
Found: C, 54.36; H, 4.56; N, 22.65.

MS(EI): 303 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.85 (3H, s), 3.20-3.80 (3H, br.s), 5.15 (1H, s), 6.81 (1H, s), 7.16-7.028 (3H, m), 7.34 (1H, d, $J=7.3$ Hz),
15 10.05-11.07 (2H, brs).

Example 10

4-(2-Fluorophenyl)-4,7-dihydro-6-methyl-5-isopropylthiocarbonyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and acetoacetic acid isopropyl thioester in the same manner as in Example 1.

MP:192-194°C.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.03 (3H, d, $J=6.9$ Hz), 1.15 (3H, d, $J=6.9$ Hz), 2.43 (3H, s), 3.35 (1H, q, $J=6.9$ Hz), 5.55 (1H, s),
25 7.04-7.15 (4H, m), 7.33 (1H, s), 9.81 (1H, br.s), 12.11 (1H, br.s).

Example 11

4,7-Dihydro-6-methyl-5-nitro-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and 1-nitropropan-2-one in the same manner as in Example 1.

MP:257-258°C.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.65 (3H, s), 5.75 (1H, s),

7.19(1H,s), 7.30-7.35(2H,m), 7.51(1H,dd,J=7.3Hz and 7.8Hz),
7.66(1H,d,J=7.8Hz), 10.87(1H,br.s), 12.45(1H,br.s).

Example 12

Ethyl 4,7-dihydro-4-phenyl-6-trifluoromethyl-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

The title compound was prepared from benzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:110-115°C.

10 Anal. Calcd. for: $C_{16}H_{14}N_3O_2F_3 \cdot 1/2 H_2O$: C, 55.49; H, 4.37; N, 12.13.

Found: C, 55.84; H, 4.70; N, 11.89.

MS(EI): 337 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.84(3H,t,J=6.9Hz),
3.90(2H,q,J=6.8Hz), 5.54(1H,s), 7.13-7.17(3H,m), 7.24-
15 7.28(3H,m), 9.78(1H,br.s), 12.20(1H,br.s).

IR(KBr): ν =3375, 3175, 3067, 1707, 1606, 1533, 1278, 1206, 1197, 1167 cm^{-1} .

Example 13

Ethyl 4-(2-fluorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:119-120°C.

Anal. Calcd. for: $C_{16}H_{13}F_4N_3O_2$: C, 54.09; H, 3.69; N, 11.84.

25 Found: C, 53.84; H, 3.57; N, 11.79.

MS(EI): 356 ($M^+ + 1$).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H,t,J=6.8Hz),
3.89(2H,q,J=6.8Hz), 5.46(1H,s), 7.11-7.20(4H,m), 7.28-
7.30(1H,m), 9.92(1H,br.s), 12.27(1H,br.s).

30 IR(KBr): ν =3290, 3178, 3069, 1703, 1608, 1537, 1280, 1232, 1174, 1138,
756 cm^{-1} .

Example 14

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

5 MP:171-172°C.

MS(EI):371 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91 (3H, t, J=7.3Hz),
3.50 (3H, br.s), 3.87 (2H, q, J=6.8Hz), 5.66 (1H, s), 6.26 (2H, s),
7.15-7.18 (2H, m), 7.27 (1H, d, J=7.8Hz), 7.30 (1H, s),
10 7.40 (1H, d, J=7.8Hz), 9.65 (1H, br.s).

IR(KBr):ν=3297, 2935, 1730, 1624, 1550, 1479, 1186cm⁻¹.

Example 15

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:144-146°C.

Anal. Calcd. for: C₁₇H₁₆F₃N₃O₃: C, 55.59; H, 4.39; N, 11.44.

20 Found: C, 55.55; H, 4.38; N, 11.43.

MS(EI):367 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94 (3H, t, J=6.8Hz), 3.83 (3H, s),
3.89 (2H, q, J=6.8Hz), 5.51 (1H, s), 6.84 (1H, dd, J=7.3Hz and 7.4Hz),
6.94-6.97 (2H, m), 7.13 (1H, dd, J=7.3Hz and 7.4Hz), 7.20 (1H, s),
25 9.70 (1H, br.s), 12.13 (1H, br.s).

IR(KBr):ν=3431, 3173, 3067, 2993, 2924, 1689, 1610, 1527, 1286, 1226,
1145cm⁻¹.

Example 16

Ethyl 4,7-dihydro-6-trifluoromethyl-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl

trifluoroacetoacetate in the same manner as in Example 1.

MP:182-186°C.

Anal. Calcd. for: $C_{17}H_{13}N_3O_2F_6$: C, 50.38; H, 3.23; N, 10.37.

Found: C, 50.21; H, 3.15; N, 10.39.

5 MS (FAB): 406 ($M^+ + 1$).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83 (3H, t, J=6.8Hz),
3.83 (2H, q, J=6.8Hz), 5.49 (1H, s), 7.08 (1H, s), 7.35-7.39 (2H, m),
7.62 (1H, dd, J=7.3Hz and 7.4Hz), 7.66 (1H, d, J=7.8Hz),
9.97 (1H, br.s), 12.30 (1H, br.s).

10 IR (KBr): ν =3339, 3177, 3067, 1711, 1608, 1537, 1313, 1280, 1182, 1141 cm^{-1} .

Example 17

Ethyl 4-(3-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-
15 chlorobenzaldehyde, 3-aminopyrazole and ethyl
trifluoroacetoacetate in the same manner as in Example 1.

MP:144-145°C.

Anal. Calcd. for: $C_{16}H_{13}N_3O_2F_3Cl$: C, 51.69; H, 3.52; N, 11.30.

Found: C, 51.33; H, 3.74; N, 11.10.

20 MS (EI): 371 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.98 (3H, t, J=6.8Hz),
3.92 (2H, q, J=6.8Hz), 5.21 (1H, s), 7.11 (1H, d, J=7.8Hz), 7.17 (1H, s),
7.23 (1H, d, J=8.7Hz), 7.29-7.33 (2H, m), 9.92 (1H, br.s),
12.30 (1H, br.s).

25 IR (KBr): ν =3321, 3178, 3070, 1703, 1610, 1535, 1278, 1224, 1184, 1145 cm^{-1} .

Example 18

Ethyl 4-(4-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 4-
30 chlorobenzaldehyde, 3-aminopyrazole and ethyl
trifluoroacetoacetate in the same manner as in Example 1.

MP:176-178°C.

Anal. Calcd. for: $C_{16}H_{13}F_3N_3O_2Cl$: C, 51.69; H, 3.52; N, 11.30.

Found: C, 51.91; H, 3.77; N, 11.08.

MS (EI): 371 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.98 (3H, t, $J=6.8\text{Hz}$),
3.90 (2H, q, $J=7.3\text{Hz}$), 5.92 (1H, s), 7.16 (2H, d, $J=8.2\text{Hz}$), 7.27 (1H, s),
5 7.31 (2H, d, $J=8.2\text{Hz}$), 9.87 (1H, br.s), 12.27 (1H, br.s).

IR (KBr): $\nu=3476, 3368, 3178, 3078, 1714, 1695, 1606, 1537, 1278, 1172,$
1134 cm^{-1} .

Example 19

Ethyl 4,7-dihydro-4-(4-methoxyphenyl)-6-trifluoromethyl-2H-
10 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 4-methoxybenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP: 159-161°C.

15 Anal. Calcd. for: $\text{C}_{17}\text{H}_{16}\text{FN}_3\text{O}_3$: C, 55.59; H, 4.39; N, 11.44.

Found: C, 55.49; H, 4.54; N, 11.33.

MS (EI): 367 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.99 (3H, t, $J=7.3\text{Hz}$), 3.68 (3H, s),
3.89 (2H, q, $J=7.3\text{Hz}$), 5.12 (1H, s), 6.82 (2H, d, $J=8.7\text{Hz}$),
20 7.03 (2H, d, $J=8.7\text{Hz}$), 7.22-7.24 (1H, m), 9.71 (1H, br.s),
12.19 (1H, br.s).

IR (KBr): $\nu=3323, 3231, 3173, 3067, 1699, 1610, 1535, 1510, 1302, 1248, 1184,$
1145 cm^{-1} .

Example 20

25 Ethyl 4-(4-ethoxycarbonylphenyl)-4,7-dihydro-6-
trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 4-ethoxycarbonylbenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

30 MP: 157-160°C.

Anal. Calcd. for: $\text{C}_{19}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_4$: C, 55.75; H, 4.43; N, 10.26.

Found: C, 55.68; H, 4.39; N, 10.43.

MS (FAB): 410 (M^++1).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.96 (3H, t, J=6.9Hz), 1.28 (3H, t, J=7.3Hz), 3.89 (2H, q, J=6.8Hz), 4.27 (2H, q, J=7.3Hz), 5.28 (1H, s), 7.27 (1H, s), 7.29 (2H, d, J=8.3Hz), 7.87 (2H, d, J=8.2Hz), 9.92 (1H, br.s), 12.28 (1H, br.s).

5 IR(KBr): ν=3393, 3188, 3082, 1692, 1612, 1539, 1284 cm⁻¹.

Example 21

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-3-methyl-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-amino-5-methylpyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP: 165-168°C.

MS(EI): 385 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94 (3H, t, J=7.3Hz), 1.81 (3H, s), 3.85 (2H, q, J=6.8Hz), 5.54 (1H, s), 7.17-7.20 (2H, m), 7.27 (1H, dd, J=7.3Hz and 7.4Hz), 7.36 (1H, d, J=8.3Hz), 9.79 (1H, br.s), 11.96 (1H, br.s).

IR(KBr): ν=3263, 3194, 3080, 1668, 1591, 1520, 1286, 1232, 1149, 1095, 1062 cm⁻¹.

20 Example 22

Ethyl 4,7-dihydro-4-(thiophen-2-yl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from thiophene-2-aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP: 157-161°C.

Anal. Calcd. for: C₁₄H₁₂F₃N₃O₂S: C, 49.27; H, 2.95; N, 12.31.

Found: C, 49.10; H, 3.28; N, 12.13.

MS(EI): 343 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.08 (3H, t, J=7.4Hz), 4.00 (2H, q, J=7.4Hz), 5.52 (1H, s), 6.76 (1H, d, J=2.9Hz), 6.87 (1H, dd, J=2.9Hz and 5.4Hz), 7.30 (1H, d, J=5.4Hz), 7.43 (1H, s), 9.96 (1H, br.s), 12.35 (1H, br.s).

IR(KBr): ν =3350, 3240, 3180, 1693, 1612, 1535, 1396, 1371, 1304, 1153, 1093, 1057, 694 cm^{-1} .

Example 23

Ethyl 4,7-dihydro-4-(thiophen-3-yl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from thiophene-3-aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP: 140-145°C.

10 Anal. Calcd. for: $\text{C}_{14}\text{H}_{12}\text{F}_3\text{N}_3\text{O}_2\text{S}$: C, 49.27; H, 2.95; N, 12.31.

Found: C, 49.65; H, 2.64; N, 12.19.

MS(EI): 343 (M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.03 (3H, t, $J=7.3\text{Hz}$), 3.96 (2H, q, $J=7.3\text{Hz}$), 5.30 (1H, s), 6.87 (1H, d, $J=4.8\text{Hz}$), 7.05 (1H, s),
15 7.35 (1H, s), 7.39 (1H, dd, $J=2.9\text{Hz}$ and 4.8Hz), 9.76 (1H, br.s), 12.25 (1H, br.s).

IR(KBr): ν =3356, 3182, 2982, 2932, 1689, 1614, 1537, 1304, 1224, 1153 cm^{-1} .

Example 24

Ethyl 4,7-dihydro-4-(1-naphthyl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from naphthalene-1-aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP: 119-120°C.

25 Anal. Calcd. for: $\text{C}_{20}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2 \cdot 1/2 \text{H}_2\text{O}$: C, 60.45; H, 4.57; N, 10.57.

Found: C, 60.20; H, 4.77; N, 10.39.

MS(FAB): 388 (M^++1).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.69 (3H, t, $J=6.8\text{Hz}$), 3.73 (2H, q, $J=6.8\text{Hz}$), 6.04 (1H, s), 7.09 (1H, s), 7.26 (1H, d, $J=6.8\text{Hz}$),
30 7.41 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz), 7.52-7.58 (2H, m), 7.75 (1H, d, $J=8.3\text{Hz}$), 7.92 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz), 8.33 (1H, s), 9.87 (1H, br.s), 12.14 (1H, br.s).

IR(KBr): ν =3173, 1670, 1606, 1138, 1095 cm^{-1} .

Example 25

Ethyl 4,7-dihydro-4-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

A solution of benzaldehyde (1.6 g), 3-aminopyrazole (1.0 g) and ethyl 3-ketohexanoate (1.9 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (720 mg) as colorless crystals.

MP: 139-141°C.

Anal. Calcd. for: $C_{18}H_{21}N_3O_2 \cdot C_4H_4O_4 \cdot \frac{1}{2} H_2O$: C, 60.54; H, 6.00; N, 9.63.

Found: C, 60.16; H, 5.60; N, 10.01.

MS (EI): 311 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94-0.95 (6H, m), 1.62 (2H, q, $J=7.8$ Hz), 2.66-2.77 (2H, m), 3.50 (3H, br. s), 3.83 (2H, q, $J=6.8$ Hz), 5.10 (1H, s), 6.25 (2H, s), 7.05-7.20 (6H, m), 9.37 (1H, br. s).

IR (KBr): $\nu=3337, 3042, 1699, 1593, 1467, 1539, 1361, 1203$ cm $^{-1}$

Example 26

Ethyl 4-(2-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 192-194°C.

Anal. Calcd. for: $C_{18}H_{20}FN_3O_2 \cdot \frac{1}{2} H_2O$: C, 63.89; H, 6.26; N, 12.42.

Found: C, 63.85; H, 6.01; N, 12.36.

MS (EI): 329 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H, t, $J=7.3$ Hz), 0.97 (3H, t, $J=7.3$ Hz), 1.62-1.68 (2H, m), 2.71-2.83 (2H, m), 3.82 (2H, q, $J=7.3$ Hz), 5.43 (1H, s), 7.05-7.11 (4H, m), 7.21 (1H, s),

9.48(1H,br.s), 11.97(1H,br.s).

IR(KBr): ν =3265,3198,2964,1591,1514,1224,1209,1093 cm^{-1} .

Example 27

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:202-205°C.

10 Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{ClN}_3\text{O}_2$:C,62.52;H,5.83;N,12.15.

Found:C,62.28;H,5.76;N,12.37.

MS(FAB):346(M^+ +1).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.85 (3H,t,J=6.8Hz), 0.95
(3H,t,J=7.3Hz), 1.62-1.68(2H,m), 2.67-2.87(2H,m),
15 3.78(2H,q,J=6.8Hz), 5.58(1H,s), 7.07-7.11(2H,m),
7.18(1H,dd,J=7.3Hz and 7.4Hz), 7.25(1H,s), 7.34(1H,d,J=7.8Hz),
9.49(1H,br.s), 11.97(1H,br.s).
IR(KBr): ν =3263,3209,3194,3080,1668,1591,1520,1286,1232,1149,1062,
750 cm^{-1} .

20 Example 28

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl 3-ketohexanoate
25 in the same manner as in Example 25.

MP:203-207°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{18}\text{ClN}_3\text{O}_2 \cdot 1/5 \text{H}_2\text{O}$:C,60.88;H,5.53;N,12.53.

Found:C,60.73;H,5.36;N,12.14.

MS(EI):331(M^+).

30 ^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.97 (3H,t,J=7.3Hz), 1.64-
1.66(2H,m), 2.72-2.83(2H,m), 3.31(3H,s), 5.57(1H,s),
7.10(1H,d,J=7.3Hz), 7.09-7.11(1H,m), 7.17-7.18(1H,m),
7.27(1H,s), 7.34(1H,d,J=7.8Hz), 9.54(1H,br.s), 11.97(1H,br.s).

IR(KBr): ν =3260, 3190, 1672, 1591, 1516, 1232 cm^{-1} .

Example 29

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was prepared from 2-bromobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 223°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{BrN}_3\text{O}_2$: C, 55.40; H, 5.17; N, 10.77.

10 Found: C, 55.08; H, 5.14; N, 10.85.

MS(EI): 390 (M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.86 (3H, t, $J=7.3\text{Hz}$),
0.97 (3H, t, $J=7.3\text{Hz}$), 1.63-1.69 (2H, m), 2.71-2.74 (1H, m), 2.80-
2.83 (1H, m), 3.77 (2H, q, $J=7.3\text{Hz}$), 5.67 (1H, s), 7.00 (1H, dd, $J=7.3\text{Hz}$
15 and 7.4Hz), 7.10 (1H, d, $J=7.3\text{Hz}$), 7.22 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz),
7.28 (1H, s), 7.51 (1H, d, $J=7.3\text{Hz}$), 9.50 (1H, br.s), 11.97 (1H, br.s).

Example 30

Ethyl 4,7-dihydro-4-(2-methylphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 178°C.

Anal. Calcd. for: $\text{C}_{19}\text{H}_{23}\text{N}_3\text{O}_2$: C, 70.13; H, 7.12; N, 12.91.

25 Found: C, 70.12; H, 7.35; N, 12.99.

MS(EI): 325 (M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83 (3H, t, $J=7.3\text{Hz}$),
0.96 (3H, t, $J=7.3\text{Hz}$), 1.62-1.66 (2H, m), 2.44 (3H, s), 2.64-
2.66 (1H, m), 2.76-2.79 (1H, m), 3.77 (2H, q, $J=7.3\text{Hz}$), 5.31 (1H, s),
30 6.93 (1H, d, $J=7.3\text{Hz}$), 6.99-7.05 (3H, m), 7.18 (1H, s), 9.34 (1H, br.s),
11.87 (1H, br.s).

Example 31

Ethyl 4,7-dihydro-6-propyl-4-(2-trifluoromethylphenyl)-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:198-202°C.

Anal. Calcd. for: $C_{19}H_{20}F_3N_3O_2 \cdot \frac{1}{2} H_2O$: C, 58.76; H, 5.45; N, 10.81.

Found: C, 58.82; H, 5.92; N, 10.62.

MS (EI) : 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.76 (3H, t, J=7.3Hz),
10 0.98 (3H, t, J=7.3Hz), 1.64-1.68 (2H, m), 2.76-2.79 (2H, m),
3.80 (2H, q, J=7.3Hz), 5.44 (1H, s), 7.00 (1H, s), 7.27-7.30 (1H, m),
7.33 (1H, d, J=7.8Hz), 7.53 (1H, dd, J=7.3Hz and 7.4Hz),
7.61 (1H, d, J=7.3Hz), 9.54 (1H, br. s), 11.99 (1H, br. s).
IR (KBr) : ν =3265, 3198, 2964, 1591, 1514, 1224, 1209, 1093 cm^{-1} .

15 **Example 32**

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
20 in the same manner as in Example 25.

MP:169°C.

Anal. Calcd. for: $C_{19}H_{23}N_3O_3$: C, 66.84; H, 6.79; N, 12.31.

Found: C, 66.58; H, 6.50; N, 12.34.

MS (EI) : 341 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 1.66-1.68 (2H, m), 2.66-2.70 (1H, m), 2.81-
2.88 (1H, m), 3.80 (2H, q, J=7.3Hz), 3.85 (3H, s), 5.47 (1H, s),
6.76 (1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94 (2H, m),
7.04 (1H, dd, J=7.3Hz and 7.4Hz), 7.14 (1H, s), 9.29 (1H, br. s),
30 11.82 (1H, br. s).

Example 33

Ethyl 4-(2-ethoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-ethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:203°C.

5 Anal. Calcd. for: $C_{20}H_{25}N_3O_3$: C, 67.58; H, 7.09; N, 11.82.

Found: C, 67.48; H, 7.06; N, 11.81.

MS (EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 1.41 (3H, t, J=7.3Hz), 1.64-1.67 (2H, m), 2.68-
10 2.71 (1H, m), 2.78-2.81 (1H, m), 3.79 (2H, q, J=7.3Hz), 4.03-
4.05 (1H, m), 4.10-4.12 (1H, m), 5.48 (1H, s), 6.74 (1H, dd, J=7.3Hz
and 7.4Hz), 6.87 (1H, d, J=7.3Hz), 6.94 (1H, d, J=7.3Hz),
7.01 (1H, dd, J=7.3Hz and 7.4Hz), 7.14 (1H, s), 9.28 (1H, br.s),
11.79 (1H, br.s).

15 Example 34

Ethyl 4,7-dihydro-4-(2-propoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-propoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
20 in the same manner as in Example 25.

MP:205°C.

Anal. Calcd. for: $C_{21}H_{27}N_3O_3$: C, 68.27; H, 7.37; N, 11.37.

Found: C, 68.05; H, 7.39; N, 11.35.

MS (EI): 369 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.84 (3H, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 1.05 (3H, t, J=7.3Hz), 1.64-1.67 (2H, m), 1.81-
1.84 (2H, m), 2.70-2.73 (1H, m), 2.78-2.82 (1H, m),
3.77 (2H, q, J=7.3Hz), 3.92 (1H, q, J=7.3Hz), 4.07 (1H, q, J=7.3Hz),
5.52 (1H, s), 6.75 (1H, dd, J=7.3Hz and 7.4Hz), 6.88 (1H, d, J=7.3Hz),
30 6.94 (1H, d, J=7.3Hz), 7.01 (1H, dd, J=7.3Hz and 7.4Hz), 7.11 (1H, s),
9.28 (1H, br.s), 11.79 (1H, br.s).

Example 35

Ethyl 4,7-dihydro-4-(2-isopropoxyphenyl)-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-isopropoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:210°C.

Anal. Calcd. for: C₂₁H₂₇N₃O₃: C, 68.27; H, 7.37; N, 11.37.

Found: C, 67.93; H, 7.39; N, 11.32.

MS (EI): 369 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.84 (3H, t, J=7.3Hz),
10 0.97 (3H, t, J=7.3Hz), 1.25 (3H, d, J=6.8Hz), 1.39 (3H, d, J=6.8Hz),
1.64-1.69 (2H, m), 2.68-2.72 (1H, m), 2.78-2.82 (1H, m),
3.77 (2H, q, J=7.3Hz), 4.64-4.67 (1H, m), 5.45 (1H, s),
6.73 (1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.90 (3H, m), 7.15 (1H, s),
9.27 (1H, br.s), 11.77 (1H, br.s).

15 **Example 36**

Ethyl 4-(2-butoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-butoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
20 in the same manner as in Example 25.

MP:171°C.

Anal. Calcd. for: C₂₂H₂₉N₃O₃: C, 68.90; H, 7.62; N, 10.96.

Found: C, 68.66; H, 7.63; N, 10.89.

MS (EI): 383 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.84 (3H, t, J=7.3Hz), 0.95-
0.99 (6H, m), 1.52-1.80 (6H, m), 2.69-2.71 (1H, m), 1.76-1.80 (1H, m),
3.77 (2H, q, J=7.3Hz), 3.95-3.98 (1H, m), 4.07-4.10 (1H, m),
5.51 (1H, s), 6.74 (1H, dd, J=7.3Hz and 7.4Hz), 6.88-6.94 (2H, m),
7.01 (1H, dd, J=7.3Hz and 7.4Hz), 7.10 (1H, s), 9.28 (1H, br.s),
30 11.79 (1H, br.s).

Example 37

Ethyl 4-(2-cyclopentyloxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-cyclopentyloxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:195°C.

5 Anal. Calcd. for: $C_{23}H_{29}N_3O_3$: C, 69.85; H, 7.39; N, 10.62.

Found: C, 69.63; H, 7.28; N, 10.61.

MS (EI): 395 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83 (3H, t, $J=7.3$ Hz),
0.97 (3H, t, $J=7.3$ Hz), 1.65-1.98 (8H, m), 2.66-2.78 (2H, m),
10 3.76 (2H, q, $J=7.3$ Hz), 4.89-4.93 (1H, m), 5.43 (1H, s),
6.72 (1H, dd, $J=7.3$ Hz and 7.4Hz), 6.88-6.93 (2H, m),
7.00 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.10 (1H, s), 9.28 (1H, br.s),
11.77 (1H, br.s).

Example 38

15 Ethyl 4-(2-benzyloxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-benzyloxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

20 MP:128°C.

Anal. Calcd. for: $C_{25}H_{27}N_3O_3$: C, 71.92; H, 6.52; N, 10.06.

Found: C, 71.66; H, 6.73; N, 9.85.

MS (EI): 417 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.84 (3H, t, $J=7.3$ Hz),
25 0.97 (3H, t, $J=7.3$ Hz), 1.64-1.67 (2H, m), 2.70-2.73 (1H, m), 2.80-
2.83 (1H, m), 3.80 (2H, q, $J=7.3$ Hz), 5.20 (2H, d, $J=30$ Hz), 5.60 (1H, s),
6.78 (1H, dd, $J=7.3$ Hz and 7.4Hz), 6.96-7.03 (3H, m), 7.08 (1H, s),
7.35 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.40-7.43 (2H, m), 7.52-
7.55 (2H, m), 9.30 (1H, br.s), 11.79 (1H, br.s).

30 Example 39

Ethyl 4,7-dihydro-4-(2-methylthiophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of 2-methylthiobenzaldehyde (20 g), Meldrum's

acid (19 g), ethyl 3-ketohexanoate (21 g) and ammonium acetate (11 g) in acetic acid (130 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give
5 colorless crystals (9.7 g). To a solution of dimethylformamide (1.3 g) in chloroform (5 mL) were added phosphorus oxychloride (1.7 mL) and a solution of the obtained colorless crystals (1.5 g) in chloroform (10 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous
10 sodium acetate (18.5 g) solution was added and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate
15 (8:2)) to give colorless crystals (0.9 g). To a solution of the obtained colorless crystals (0.9 g) in pyridine (10 mL) was added hydrazine (0.27 g) and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced
20 pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (230 mg) as colorless crystals.

MP:198°C.

Anal. Calcd. for: $C_{19}H_{23}N_3O_2S$: C, 63.84; H, 6.49; N, 11.75.

25 Found: C, 63.56; H, 6.45; N, 11.64.

MS(EI): 357 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82 (3H, t, $J=7.3$ Hz),
0.96 (3H, t, $J=7.3$ Hz), 1.62-1.68 (2H, m), 2.48 (3H, s), 2.67-
2.71 (1H, m), 2.79-2.83 (1H, m), 3.74 (2H, q, $J=7.3$ Hz), 5.54 (1H, s),
30 6.99-7.06 (3H, m), 7.22-7.25 (2H, m), 9.38 (1H, br.s),
11.86 (1H, br.s).

Example 40

Ethyl 4,7-dihydro-4-(2-methylsulfinylphenyl)-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of ethyl 4,7-dihydro-4-(2-methylthio)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (100 mg) in tetrahydrofuran (3.0 mL) was added metachloroperbenzoic acid (60 mg) and the mixture was stirred at -78°C for 30 minutes. An aqueous sodium thiosulfate solution was added, and the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give colorless crystals. By recrystallization from ethyl acetate, the title compound (50 mg) was obtained as colorless crystals.

MP:216°C.

Anal. Calcd. for: C₁₉H₂₃N₃O₃S: C, 61.10; H, 6.21; N, 11.25.

Found: C, 61.32; H, 6.18; N, 10.99.

MS (EI): 373 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.91 (3H, t, J=7.3Hz), 0.97 (3H, t, J=7.3Hz), 1.64-1.68 (2H, m), 2.69-2.72 (1H, m), 2.72 (3H, s), 2.76-2.79 (1H, m), 3.90 (2H, q, J=7.3Hz), 5.36 (1H, s), 7.15 (1H, dd, J=7.3Hz and 7.4Hz), 7.20 (1H, s), 7.37-7.39 (2H, m), 7.85 (1H, dd, J=7.3Hz and 7.4Hz), 9.59 (1H, br.s), 12.04 (1H, br.s).

Example 41

Ethyl 4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-nitrobenzaldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:218°C.

Anal. Calcd. for: C₁₈H₂₀N₄O₄: C, 60.66; H, 5.66; N, 15.72.

Found: C, 60.25; H, 5.65; N, 15.44.

MS (EI): 356 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.80 (3H, t, J=7.3Hz), 0.95 (3H, t, J=7.3Hz), 1.59-1.64 (2H, m), 2.69-2.73 (1H, m), 2.77-2.80 (1H, m), 3.72 (2H, q, J=7.3Hz), 5.45 (1H, s), 7.28-7.33 (3H, m), 7.56 (1H, dd, J=7.3Hz and 7.4Hz), 7.76 (1H, d, J=7.3Hz), 9.64 (1H, br.s), 10.07 (1H, br.s).

Example 42

Ethyl 4-(2-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-cyanobenzaldehyde
5 and ethyl 3-ketohexanoate in the same manner as in Example 39.
MP:211°C.

Anal. Calcd. for: $C_{19}H_{20}N_4O_2$: C, 67.84; H, 5.99; N, 16.66.

Found: C, 67.49; H, 6.14; N, 16.23.

MS(EI): 336 (M^+).

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, J=7.3Hz),
0.94 (3H, t, J=7.3Hz), 1.61-1.67 (2H, m), 2.71-2.73 (1H, m), 2.79-
2.82 (1H, m), 3.80 (2H, q, J=7.3Hz), 5.48 (1H, s), 7.21-7.29 (2H, m),
7.28 (1H, dd, J=7.3Hz and 7.4Hz), 7.55 (1H, dd, J=7.3Hz and 7.4Hz),
7.70 (1H, d, J=7.3Hz), 9.63 (1H, br.s), 12.07 (1H, br.s).

15 **Example 43**

Ethyl 4-(2,3-difluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-
difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-
20 ketohexanoate in the same manner as in Example 25.

MP:207°C.

Anal. Calcd. for: $C_{18}H_{19}F_2N_3O_2 \cdot 1/5 H_2O$: C, 61.60; H, 5.57; N, 11.97.

Found: C, 61.41; H, 5.56; N, 11.59.

MS(EI): 347 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.97 (6H, m), 1.60-1.66 (2H, m),
2.68-2.71 (1H, m), 2.79-2.82 (1H, m), 3.83 (2H, q, J=7.3Hz),
5.45 (1H, s), 6.87 (1H, dd, J=7.3Hz and 7.4Hz), 7.03-7.13 (2H, m),
7.76 (1H, s), 9.55 (1H, br.s), 12.03 (1H, br.s).

Example 44

30 Ethyl 4-(2,3-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-
dichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-

ketohehexanoate in the same manner as in Example 25.

MP:220°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2$: C, 56.85; H, 5.04; N, 11.05.

Found: C, 56.35; H, 5.00; N, 11.01.

5 MS (EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88 (3H, t, $J=7.3$ Hz),
0.99 (3H, t, $J=7.3$ Hz), 1.66-1.69 (2H, m), 2.74-2.77 (1H, m), 2.82-
2.86 (1H, m), 3.81 (2H, q, $J=7.3$ Hz), 5.66 (1H, s), 7.10 (1H, d, $J=7.3$ Hz),
7.24 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.31 (1H, s), 7.38 (1H, d, $J=7.3$ Hz),
10 9.59 (1H, br. s), 12.04 (1H, br. s).

Example 45

Ethyl 4-(3-fluoro-2-methylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-fluoro-2-
15 methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohehexanoate
in the same manner as in Example 25.

MP:159-162°C.

Anal. Calcd. for: $C_{19}H_{22}FN_3O_3 \cdot 3/10 H_2O$: C, 65.42; H, 6.53; N, 12.05.

Found: C, 65.56; H, 6.29; N, 12.40.

20 MS (EI): 343 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.3$ Hz), 0.97
(3H, t, $J=7.3$ Hz), 1.64 (2H, m), 2.36 (3H, s), 2.67-2.84 (2H, m),
3.80 (2H, q, $J=7.3$ Hz), 5.35 (1H, s), 6.86 (2H, d, $J=8.8$ Hz),
7.07 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.23 (1H, s), 9.42 (1H, br. s),
25 11.94 (1H, br. s).

IR (KBr): $\nu=3265, 3193, 2966, 2934, 1668, 1591, 1520, 1466, 1240$ cm^{-1} .

Example 46

Ethyl 4-(2,3-dimethoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2,3-
dimethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-
ketohehexanoate in the same manner as in Example 25.

MP:205-206°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31.

Found: C, 64.76; H, 6.81; N, 11.15.

MS (EI): 371 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90 (3H, t, $J=7.4$ Hz),
5 0.98 (3H, t, $J=7.3$ Hz), 1.66-1.68 (2H, m), 2.68-2.70 (1H, m), 2.80-
2.83 (1H, m), 3.77 (3H, s), 3.80 (3H, s), 3.80-3.85 (2H, m),
5.44 (1H, s), 6.58 (1H, d, $J=7.3$ Hz), 6.76 (1H, d, $J=6.8$ Hz),
6.88 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.11 (1H, s), 9.32 (1H, br. s),
11.83 (1H, br. s).

10 Example 47

Ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-3-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl 3-
15 ketoheptanoate in the same manner as in Example 25.

MP: 236-238°C.

Anal. Calcd. for: $C_{19}H_{19}ClF_3N_3O_2$: C, 55.15; H, 4.63; N, 10.15.

Found: C, 55.07; H, 4.55; N, 10.13.

MS (EI): 413 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82 (3H, t, $J=7.3$ Hz),
0.97 (3H, t, $J=7.3$ Hz), 1.65 (2H, m), 2.70-2.90 (2H, m), 3.65-
3.85 (2H, m), 5.72 (1H, s), 7.29 (1H, s), 7.41-7.42 (2H, m), 7.59-
7.61 (1H, m), 9.62 (1H, br. s), 12.05 (1H, br. s).

Example 48

25 Ethyl 4-(2-chloro-4-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-4-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 25.

30 MS (EI): 363 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88 (3H, t, $J=7.3$ Hz),
0.96 (3H, t, $J=7.3$ Hz), 1.62-1.67 (2H, m), 2.66-2.80 (2H, m),
3.77 (2H, q, $J=7.3$ Hz), 5.54 (1H, s), 7.08-7.13 (2H, m), 7.25 (1H, s),

7.32 (1H, dd, J=2.5Hz and 8.8Hz), 9.53 (1H, br.s), 11.99 (1H, br.s).

Example 49

Ethyl 4-(2,5-difluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was prepared from 2,5-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 168-169°C.

MS (EI): 347 (M⁺).

10 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.92-0.99 (6H, m), 1.62-1.68 (2H, m), 2.67-2.71 (1H, m), 2.85-2.88 (1H, m), 3.80-3.91 (2H, m), 4.03 (1H, q, J=6.8Hz), 5.40 (1H, s), 6.77-6.80 (1H, m), 6.98-7.00 (1H, m), 7.12-7.16 (1H, m), 7.26 (1H, s), 9.59 (1H, br.s), 12.06 (1H, br.s).

15 **Example 50**

Ethyl 4-(2,5-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-dichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 162°C.

Anal. Calcd. for: C₁₈H₁₉Cl₂N₃O₂ 1/2 H₂O: C, 55.54; H, 5.18; N, 10.79.

Found: C, 55.50; H, 5.50; N, 11.17.

MS (EI): 380 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.89 (3H, t, J=7.3Hz), 0.98 (3H, t, J=7.3Hz), 1.62-1.66 (2H, m), 2.64-2.67 (1H, m), 2.86-2.90 (1H, m), 3.81 (2H, q, J=7.3Hz), 5.55 (1H, s), 7.04 (1H, s), 7.18 (1H, d, J=7.3Hz), 7.28 (1H, s), 7.41 (1H, d, J=7.3Hz), 9.61 (1H, br.s), 12.06 (1H, br.s).

30 **Example 51**

Ethyl 4-(5-fluoro-2-methoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 5-fluoro-2-

methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:164-167°C.

Anal. Calcd. for: $C_{19}H_{22}FN_3O_3$: C, 63.50; H, 6.17; N, 11.69.

5 Found: C, 63.24; H, 6.09; N, 11.70.

MS (EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, J=7.3Hz),
0.98 (3H, t, J=7.3Hz), 1.64-1.69 (2H, m), 2.62-2.91 (2H, m),
3.79 (2H, q, J=7.3Hz), 3.85 (3H, s), 5.44 (1H, s), 6.33 (1H, dd, J=3.0Hz
10 and 7.8Hz), 6.83-6.91 (2H, m), 7.17 (1H, s), 9.41 (1H, br. s),
11.89 (1H, br. s).

IR (KBr): ν =3252, 2955, 1657, 1510, 1232, 1074 cm^{-1} .

Example 52

Ethyl 4-(2-chloro-5-methoxyphenyl)-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-5-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:182°C.

20 Anal. Calcd. for: $C_{19}H_{22}ClN_3O_3$: C, 60.72; H, 5.90; N, 11.18.

Found: C, 60.58; H, 5.88; N, 11.07.

MS (EI): 375 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88 (3H, t, J=7.3Hz),
0.99 (3H, t, J=7.3Hz), 1.64-1.69 (2H, m), 2.64-2.67 (1H, m), 2.87-
25 2.90 (1H, m), 3.79 (2H, q, J=7.3Hz), 3.86 (3H, s), 5.44 (1H, s),
6.85 (1H, d, J=7.3Hz), 6.94 (1H, d, J=7.3Hz), 7.10 (1H, dd, J=2.9Hz and
7.3Hz), 7.17 (1H, s), 9.43 (1H, br. s), 11.91 (1H, br. s).

Example 53

Ethyl 4-(2,5-dimethoxyphenyl)-4,7-dihydro-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-dimethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:169-170°C.

MS (EI) : 371 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88 (3H, t, J=7.3Hz),
0.98 (3H, t, J=7.3Hz), 1.68-1.70 (2H, m), 2.49-2.54 (1H, m), 2.94-
5 2.97 (1H, m), 3.57 (3H, s), 3.79-3.83 (2H, m), 3.80 (3H, s),
4.02 (1H, q, J=7.3Hz), 5.43 (1H, s), 6.49 (1H, d, J=2.9Hz),
6.59 (1H, dd, J=2.9Hz and 8.8Hz), 6.82 (1H, d, J=8.8Hz), 7.14 (1H, s),
9.32 (1H, br. s), 11.83 (1H, br. s).

Example 54

10 Ethyl 4-(2,6-difluorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,6-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

15 MP:185°C.

Anal. Calcd. for: C₁₈H₁₉F₂N₃O₂ 1/2 H₂O: C, 60.67; H, 5.66; N, 11.79.

Found: C, 60.68; H, 5.46; N, 11.61.

MS (EI) : 347 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.90-0.97 (6H, m), 1.54-1.58 (2H, m),
20 2.51-2.54 (1H, m), 2.76-2.81 (1H, m), 3.82 (2H, q, J=7.3Hz),
5.53 (1H, s), 6.90 (2H, dd, J=7.3Hz and 7.3Hz), 7.16 (1H, d, J=7.3Hz),
7.20 (1H, s), 9.50 (1H, br. s), 11.96 (1H, br. s).

Example 55

25 Ethyl 4-(2,6-dichlorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,6-dichlorobenzaldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:202°C.

30 Anal. Calcd. for: C₁₈H₁₉Cl₂N₃O₂ 3/10 H₂O: C, 56.06; H, 5.12; N, 10.90.

Found: C, 56.28; H, 5.46; N, 10.78.

MS (EI) : 380 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.83 (3H, t, J=7.3Hz),

0.92 (3H, t, J=7.3Hz), 1.57-1.62 (2H, m), 2.47-2.51 (1H, m), 2.77-2.80 (1H, m), 3.74 (2H, q, J=7.3Hz), 6.03 (1H, s), 7.05 (1H, s), 7.13 (1H, dd, J=7.3Hz and 7.4Hz), 7.22 (1H, d, J=7.3Hz), 7.39 (1H, d, J=7.3Hz), 9.53 (1H, br.s), 11.93 (1H, br.s).

5 **Example 56**

Ethyl 4-(2-chloro-6-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-6-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
10 in the same manner as in Example 25.

MP:180-183°C.

MS (EI): 363 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.92 (3H, t, J=6.9Hz),
0.94 (3H, t, J=7.3Hz), 1.56-1.61 (2H, m), 2.50-2.85 (2H, m),
15 3.80 (2H, q, J=7.3Hz), 5.75 (1H, s), 7.01-7.17 (4H, m), 9.52 (1H, br.s),
11.97 (1H, br.s).

IR (KBr): ν=3265, 1591, 1518, 1456, 1228, 1097 cm⁻¹.

Example 57

Ethyl 4,7-dihydro-6-propyl-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate dihydrochloride
20

The title compound was prepared from pyridine-3-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:251°C.

Anal. Calcd. for: C₁₇H₂₀N₄O₂·2HCl: C, 52.99; H, 5.76; N, 14.54.

25 Found: C, 52.99; H, 5.67; N, 14.44.

MS (EI): 312 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.91 (3H, t, J=7.3Hz),
1.09 (3H, t, J=7.3Hz), 1.52-1.61 (2H, m), 2.66-2.71 (2H, m), 3.93-
4.00 (2H, m), 5.24 (1H, s), 7.90 (1H, dd, J=7.3Hz and 7.4Hz), 8.31-
30 8.35 (2H, m), 8.66-8.69 (2H, m), 10.35 (1H, br.s).

Example 58

Ethyl 4,7-dihydro-6-propyl-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate dihydrochloride

The title compound was prepared from pyridine-4-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:266°C.

Anal. Calcd. for: $C_{17}H_{20}N_4O_2 \cdot 2HCl$: C, 52.99; H, 5.76; N, 14.54.

5 Found: C, 52.63; H, 5.65; N, 14.69.

MS(EI): 312 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, J=7.3Hz),
1.12 (3H, t, J=7.3Hz), 1.52-1.59 (2H, m), 2.64-2.72 (2H, m),
4.01 (2H, q, J=7.3Hz), 5.30 (1H, s), 7.76 (2H, d, J=6.4Hz), 8.66 (1H, s),
10 8.72 (2H, d, J=6.4Hz), 10.39 (1H, br.s).

Example 59

Ethyl 4-(furan-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from furan-2-aldehyde,
15 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:108-111°C.

MS(EI): 301 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, J=7.3Hz),
20 1.05 (3H, t, J=6.8Hz), 1.58 (2H, q, J=7.3Hz), 2.66-2.72 (2H, m),
3.50 (3H, br.s), 3.94 (2H, q, J=6.8Hz), 5.21 (1H, s), 5.78 (1H, d, J=2.9Hz),
6.23 (1H, s), 6.24 (2H, s), 7.75 (1H, s), 7.38 (1H, s),
9.42 (1H, br.s).

IR(KBr): ν =3207, 2962, 1703, 1479, 1348, 1205, 1076, 866 cm^{-1} .

25 Example 60

Ethyl 4-(furan-3-yl)-4,7-dihydro-4-(furan-3-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from furan-3-aldehyde,
3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
30 as in Example 25.

MP:121-123°C.

Anal. Calcd. for: $C_{16}H_{19}N_3O_3C_4H_4O_4$: C, 57.54; H, 5.55; N, 10.07.

Found: C, 57.14; H, 5.55; N, 10.37.

MS (EI) : 301 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.90 (3H, t, $J=7.3\text{Hz}$),
1.08 (3H, t, $J=7.4\text{Hz}$), 1.55-1.57 (2H, m), 2.62-2.70 (2H, m),
3.36 (1H, br. s), 3.50 (2H, br. s), 3.97 (2H, q, $J=7.3\text{Hz}$), 5.06 (1H, s),
5 6.16 (1H, s), 6.24 (2H, s), 7.13 (1H, s), 7.35 (1H, s), 7.40 (1H, s),
9.31 (1H, br. s).

IR (KBr) : $\nu=3350, 2972, 1591, 1467, 1361, 1203, 1089\text{cm}^{-1}$.

Example 61

Ethyl 4,7-dihydro-4-(2-methylfuran-3-yl)-6-propyl-2H-
10 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methylfuran-3-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 123-125°C.

15 Anal. Calcd. for: $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_3 \cdot 2/5 \text{H}_2\text{O}$: C, 63.30; H, 6.81; N, 13.03.
Found: C, 63.51; H, 6.64; N, 12.96.

MS (EI) : 315 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H, t, $J=7.3\text{Hz}$),
1.08 (3H, t, $J=7.3\text{Hz}$), 1.58-1.60 (2H, m), 2.20 (3H, s), 2.55-
20 2.75 (2H, m), 3.92 (2H, q, $J=7.3\text{Hz}$), 4.99 (1H, s), 5.96 (1H, s),
7.21 (2H, s), 9.26 (1H, br. s), 11.91 (1H, br. s).

IR (KBr) : $\nu=3265, 3198, 2964, 1591, 1514, 1224, 1209, 1093\text{cm}^{-1}$.

Example 62

Ethyl 4,7-dihydro-6-propyl-4-(thiophen-2-yl)-2H-pyrazolo[3,4-
25 b]pyridine-5-carboxylate maleate

The title compound was prepared from thiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 129-131°C.

30 Anal. Calcd. for: $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_2\text{SC}_4\text{H}_4\text{O}_4 \cdot 1/4 \text{H}_2\text{O}$: C, 54.85; H, 5.41; N, 9.59.
Found: C, 54.59; H, 5.22; N, 9.97.

MS (EI) : 317 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, $J=7.4\text{Hz}$),

1.06 (3H, t, J=7.3Hz), 1.58-1.60 (2H, m), 2.72-2.74 (2H, m),
3.50 (3H, br. s), 3.94 (2H, q, J=7.4Hz), 5.44 (1H, s), 6.25 (2H, s),
6.69 (1H, s), 6.81 (1H, d), 7.15 (1H, d), 7.37 (1H, s), 9.50 (1H, br. s).

Example 63

5 Ethyl 4,7-dihydro-4-(3-methylthiophen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-methylthiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

10 MP:125°C.

Anal. Calcd. for: C₁₇H₂₁N₃O₂S H₂O: C, 58.43; H, 6.63; N, 12.02.

Found: C, 58.59; H, 6.33; N, 12.12.

MS (EI): 331 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.96 (3H, t, J=7.4Hz),
15 0.98 (3H, t, J=7.3Hz), 1.60-1.63 (2H, m), 2.22 (3H, s), 2.83-
2.90 (2H, m), 3.88 (2H, q, J=7.3Hz), 5.42 (1H, s), 6.68 (1H, d, J=4.9Hz),
7.02 (1H, d, J=5.4Hz), 7.29 (1H, s), 9.45 (1H, br. s), 11.98 (1H, br. s).
IR (KBr): ν=3267, 3196, 2968, 1664, 1510, 1267, 1201, 1091 cm⁻¹.

Example 64

20 Ethyl 4-(5-chlorothiophen-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 5-chlorothiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

25 MP:129-131°C.

Anal. Calcd. for: C₁₆H₁₈N₃O₂SC₄H₄O₄: C, 51.33; H, 4.74; N, 8.98.

Found: C, 51.34; H, 4.54; N, 9.03.

MS (EI): 351 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.92 (3H, t, J=7.3Hz),
30 1.10 (3H, t, J=6.9Hz), 1.59-1.61 (2H, m), 2.57-2.82 (2H, m),
3.50 (2H, br. s), 3.38 (1H, s), 3.98 (2H, q, J=6.9Hz), 5.36 (1H, s),
6.25 (2H, s), 6.53 (1H, d, J=3.9Hz), 6.80 (1H, d, J=3.4Hz), 7.42 (1H, s),
9.60 (1H, br. s).

IR (KBr) : ν =3205, 2964, 2629, 1618, 1471, 1363, 1205, 1080, 889, 652 cm^{-1} .

Example 65

Ethyl 4,7-dihydro-6-propyl-4-(thiophen-3-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

5 The title compound was prepared from thiophene-3-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 141-143°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_2\text{SC}_4\text{H}_4\text{O}_4$: C, 54.42; H, 5.35; N, 9.69.

10 Found: C, 54.17; H, 5.23; N, 9.66.

MS (EI) : 317 (M^+).

^1H -NMR (400MHz, DMSO-d_6) δ (ppm): 0.92 (3H, t, $J=7.3\text{Hz}$),
1.03 (3H, t, $J=6.8\text{Hz}$), 1.59-1.61 (2H, m), 2.60-2.78 (2H, m),
3.50 (2H, br. s), 3.91 (2H, q, $J=6.8\text{Hz}$), 5.22 (2H, s), 6.26 (2H, s),
15 6.84-6.88 (2H, m), 7.29 (1H, dd, $J=3.0\text{Hz}$ and 4.9Hz), 7.33 (1H, s),
12.0 (1H, br. s).

IR (KBr) : ν =3346, 2980, 2611, 1697, 1467, 1361, 1205, 1087 cm^{-1} .

Example 66

Ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from naphthalene-1-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 182°C.

25 Anal. Calcd. for: $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2$: C, 73.11; H, 6.41; N, 11.63.

Found: C, 72.95; H, 6.47; N, 11.40.

MS (EI) : 361 (M^+).

^1H -NMR (400MHz, DMSO-d_6) δ (ppm): 0.62 (3H, t, $J=7.3\text{Hz}$),
1.00 (3H, t, $J=7.3\text{Hz}$), 1.69-1.73 (2H, m), 2.73-2.76 (1H, m), 2.84-
30 2.87 (1H, m), 3.67 (2H, q, $J=7.3\text{Hz}$), 5.95 (1H, s), 7.03 (1H, s),
7.23 (1H, d, $J=7.3\text{Hz}$), 7.36 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz),
7.49 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz), 7.57 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz),
7.65 (1H, d, $J=7.3\text{Hz}$), 7.88 (1H, d, $J=7.3\text{Hz}$), 8.40 (1H, d, $J=7.3\text{Hz}$),

9.45(1H,br.s), 11.82(1H,br.s).

Example 67

Ethyl 4,7-dihydro-4-(naphthalen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

5 The title compound was prepared from naphthalene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:136-138°C.

Anal. Calcd. for: $C_{22}H_{23}N_3O_2 \cdot C_4H_4O_4 \cdot \frac{1}{4} H_2O$: C, 64.79; H, 5.75; N, 8.72.

10 Found: C, 64.86; H, 5.57; N, 8.99.

MS(EI): 361 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92-0.98 (6H, m), 1.64-1.68 (2H, m),
2.72-2.80 (2H, m), 3.50 (2H, br.s), 3.80 (2H, q, $J=7.3$ Hz), 5.27 (1H, s),
6.25 (2H, s), 7.23 (1H, s), 7.31 (1H, d, $J=8.3$ Hz), 7.41-7.43 (2H, m),
15 7.57 (1H, s), 7.73-7.77 (2H, m), 9.47 (1H, br.s).

IR(KBr): $\nu=3202, 2962, 1701, 1464, 1359, 1222$ cm $^{-1}$.

Example 68

Ethyl 4,7-dihydro-4-(2-methoxynaphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-methoxynaphthalene-1-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:188-191°C.

Anal. Calcd. for: $C_{23}H_{25}N_3O_3 \cdot \frac{2}{5} H_2O$: C, 69.29; H, 6.52; N, 10.54.

25 Found: C, 69.35; H, 6.62; N, 10.21.

MS(EI): 391 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.71 (3H, t, $J=7.3$ Hz),
0.95 (3H, t, $J=7.3$ Hz), 1.62-1.63 (2H, m), 2.49-2.86 (2H, m),
3.61 (2H, q, $J=7.3$ Hz), 3.97 (3H, s), 6.27 (1H, s), 6.89 (1H, s), 7.16-
30 7.51 (3H, m), 7.71-7.77 (2H, m), 7.98 (1H, s), 9.43 (1H, br.s),
11.77 (1H, br.s).

IR(KBr): $\nu=3258, 1655, 1593, 1082$ cm $^{-1}$.

Example 69

Ethyl 4-(2,3-dihydrobenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dihydrobenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:194-196°C.

Anal. Calcd. for: C₂₀H₂₃N₃O₃: C, 67.97; H, 6.56; N, 11.89.

Found: C, 67.97; H, 6.68; N, 11.77.

MS (EI): 353 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.92 (3H, t, J=7.4Hz),
0.97 (3H, t, J=7.3Hz), 1.66 (2H, m), 2.67-2.70 (1H, m), 2.82-
2.84 (1H, m), 3.15 (2H, t, J=8.8Hz), 3.83-3.86 (2H, m), 4.55-
4.58 (2H, m), 5.29 (1H, s), 6.64 (1H, dd, J=7.3Hz and 7.4Hz),
6.72 (1H, d, J=6.9Hz), 6.93 (1H, dd, J=7.3Hz and 7.4Hz), 7.20 (1H, s),
9.32 (1H, br.s), 11.86 (1H, br.s).

Example 70

Ethyl 4-(5-bromo-2,3-dihydrobenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 5-bromo-2,3-dihydrobenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:200-210°C.

Anal. Calcd. for: C₂₀H₂₂BrN₃O₃: C, 55.57; H, 5.13; N, 9.72.

Found: C, 55.23; H, 5.09; N, 9.89.

MS (EI): 432 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.93-0.98 (6H, m),
1.64 (2H, q, J=7.3Hz), 2.63 (1H, m), 2.88-2.90 (1H, m),
3.16 (2H, t, J=8.3Hz), 3.85-3.87 (2H, m), 4.57-4.60 (2H, m),
5.23 (1H, s), 6.78 (1H, s), 7.11 (1H, s), 7.22 (1H, s), 9.44 (1H, br.s),
11.94 (1H, br.s).

Example 71

Ethyl 4-(5-chloro-2,3-dihydro-2-methylbenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

maleate

The title compound was prepared from 5-chloro-2,3-dihydro-2-methylbenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:155-158°C.

Anal. Calcd. for: $C_{21}H_{24}N_3O_3C_4H_4O_4$: C, 57.95; H, 5.45; N, 8.11.

Found: C, 57.57; H, 5.28; N, 8.47.

MS (EI): 401 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (6H, t, J=6.8Hz),

10 1.03 (3H, d, J=6.3Hz), 1.65 (2H, m), 2.40-2.73 (2H, m), 2.87 (1H, m),
3.29 (1H, m), 3.50 (3H, br. s), 3.84 (2H, q, J=6.8Hz), 5.05 (1H, m),
5.23 (1H, s), 6.25 (2H, s), 6.64 (1H, s), 6.95 (1H, s),
7.20 (1H, d, J=4.4Hz), 9.43 (1H, br. s).

IR (KBr): ν =3207, 2976, 1589, 1462, 1201, 1082 cm^{-1} .

15 **Example 72**

Ethyl 4-(2H-1-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2H-1-benzopyran-8-aldehyde and ethyl 3-ketohexanoate in the same manner as in

20 Example 39.

MP:194°C.

Anal. Calcd. for: $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34; N, 11.50.

Found: C, 68.60; H, 6.43; N, 11.25.

MS (EI): 194 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90 (3H, t, J=7.3Hz),
0.96 (3H, t, J=7.3Hz), 1.64-1.68 (2H, m), 2.62-2.66 (1H, m), 2.80-
2.84 (1H, m), 3.81 (2H, q, J=7.3Hz), 4.85 (2H, dd, J=2.0Hz and 9.8Hz),
5.39 (1H, s), 5.89 (1H, d, J=9.8Hz), 6.46 (1H, d, J=9.8Hz), 6.67-
6.80 (3H, m), 7.18 (1H, s), 9.31 (1H, br. s), 11.86 (1H, br. s).

30 **Example 73**

Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3,4-dihydro-2H-

benzopyran-8-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:208°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_3 \cdot \frac{1}{2} H_2O$: C, 67.01; H, 6.96; N, 11.16.

5 Found: C, 67.41; H, 6.84; N, 10.93.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 1.63-1.68 (2H, m), 1.92-1.96 (2H, m), 2.67-
2.82 (4H, m), 3.80 (2H, q, J=7.3Hz), 4.22-4.26 (2H, m), 5.41 (1H, s),
10 6.61 (1H, dd, J=7.3Hz and 7.4Hz), 6.71-6.75 (2H, m), 7.17 (1H, s),
9.25 (1H, br.s), 11.80 (1H, br.s).

Example 74

Ethyl 4,7-dihydro-6-propyl-4-(quinolin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from quinoline-4-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:198°C.

Anal. Calcd. for: $C_{21}H_{22}N_4O_2 \cdot \frac{2}{5} H_2O$: C, 68.24; H, 6.22; N, 15.16.

20 Found: C, 68.39; H, 6.04; N, 14.83.

MS(EI): 362 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.61 (3H, t, J=7.3Hz),
1.02 (3H, t, J=7.3Hz), 1.68-1.72 (2H, m), 2.76-2.78 (1H, m), 2.86-
2.89 (1H, m), 3.66-3.68 (2H, m), 5.97 (1H, s), 7.07 (1H, s),
25 7.17 (1H, d, J=4.4Hz), 7.65 (1H, dd, J=7.3Hz and 7.4Hz),
7.74 (1H, dd, J=7.3Hz and 7.4Hz), 7.99 (1H, d, J=7.3Hz),
8.48 (1H, d, J=7.8Hz), 8.73 (1H, d, J=4.4Hz), 9.61 (1H, br.s),
11.94 (1H, br.s).

Example 75

30 Ethyl 4-(benzo[b]thiophen-3-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from benzo[b]thiophene-3-aldehyde and ethyl 3-ketohexanoate in the same manner as in

Example 39.

MP:222°C.

Anal. Calcd. for: C₂₀H₂₁N₃O₂S: C, 65.37; H, 5.76; N, 11.44.

Found: C, 65.11; H, 5.31; N, 11.83.

5 MS (EI): 238 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.64 (3H, t, J=7.3Hz),
1.20 (3H, t, J=7.3Hz), 1.56-1.58 (2H, m), 2.66-2.78 (2H, m),
4.11 (2H, q, J=7.3Hz), 4.89 (1H, s), 7.42-7.50 (2H, m), 7.55 (1H, s),
7.61 (1H, s), 7.96-8.01 (2H, m), 10.32 (1H, br.s), 12.13 (1H, br.s).

10 **Example 76**

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:207°C.

Anal. Calcd. for: C₁₈H₁₉N₅O₃: C, 61.18; H, 5.42; N, 19.82.

Found: C, 61.06; H, 5.50; N, 19.66.

MS (EI): 353 (M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.77 (3H, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 2.72-2.77 (1H, m), 2.82-2.86 (1H, m),
3.79 (2H, q, J=7.3Hz), 5.68 (1H, s), 7.11 (1H, d, J=7.3Hz), 7.22 (1H, s),
7.51 (1H, dd, J=7.3Hz and 7.4Hz), 7.78 (1H, d, J=7.3Hz),
9.66 (1H, br.s), 12.01 (1H, br.s).

25 **Example 77**

Ethyl 4-(1,3-benzdioxazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 1,3-benzdioxazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:203-207°C.

Anal. Calcd. for: C₁₉H₂₁N₃O₄ 1/10 H₂O: C, 63.89; H, 5.98; N, 11.76.

Found: C, 63.72; H, 5.86; N, 12.01.

MS (EI) : 355 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 0.94 (3H, t, $J=7.3\text{Hz}$),
0.96 (3H, t, $J=7.4\text{Hz}$), 1.61-1.67 (2H, m), 2.64-2.82 (2H, m), 3.80-
3.88 (2H, m), 5.28 (1H, s), 5.99 (1H, s), 6.00 (1H, d, $J=9.7\text{Hz}$),
5 6.50 (1H, d, $J=5.9\text{Hz}$), 6.65 (1H, s), 6.65-6.69 (1H, m), 7.25 (1H, s),
9.40 (1H, br. s), 11.94 (1H, br. s) .

IR (KBr) : $\nu=3265, 3188, 2962, 1662, 1587, 1514, 1462, 1253, 1215, 1066\text{cm}^{-1}$.

Example 78

Ethyl 4-(6-chloro-3,4-dihydro-2,2-dimethyl-2H-1,4-benzoxazin-
10 8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-
carboxylate maleate

The title compound was prepared from 6-chloro-3,4-
dihydro-2,2-dimethyl-2H-1,4-benzoxazine-8-aldehyde, 3-
aminopyrazole and ethyl 3-ketohexanoate in the same manner as
15 in Example 25.

MS (EI) : 430 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 0.92 (3H, t, $J=7.4\text{Hz}$),
0.96 (3H, t, $J=7.3\text{Hz}$), 1.18 (3H, s), 1.32 (3H, s), 1.62-1.64 (2H, m),
2.66-2.82 (2H, m), 2.99 (2H, s), 3.80 (2H, t, $J=7.3\text{Hz}$), 5.32 (1H, s),
20 6.01 (2H, s), 6.14 (1H, s), 6.32 (1H, s), 7.14 (1H, s), 9.31 (1H, br. s),
11.82 (1H, br. s) .

IR (KBr) : $\nu=3281, 2974, 1672, 1599, 1520, 1207, 1155, 1091\text{cm}^{-1}$.

Example 79

Ethyl 4-(6-chloro-3,4-dihydro-2,2,4-trimethyl-1,4-benzoxazin-
25 8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-
carboxylate maleate

The title compound was prepared from 6-chloro-3,4-
dihydro-2,2,4-trimethyl-2H-1,4-benzoxazine-8-aldehyde, 3-
aminopyrazole and ethyl 3-ketohexanoate in the same manner as
30 in Example 25.

MS (EI) : 444 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 0.91 (3H, t, $J=7.3\text{Hz}$),
0.96 (3H, t, $J=7.3\text{Hz}$), 1.20 (6H, s), 1.35 (3H, s), 1.63-1.65 (2H, m),

2.83 (2H, s), 3.00 (2H, q, J=7.3Hz), 5.34 (1H, s), 6.26 (2H, s),
6.43 (1H, d, J=2.5Hz), 7.13 (1H, s), 9.33 (1H, s), 11.82 (1H, br. s).
IR (KBr): ν =3273, 2974, 1666, 1597, 1518, 1458, 1259, 1211 cm^{-1} .

Example 80

5 Ethyl 4-(2,3-dihydro-1,4-benzodioxin-6-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 2,3-dihydro-1,4-benzodioxin-6-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

10 MP: 147-149°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_4\text{C}_4\text{H}_4\text{O}_4$: C, 59.37; H, 5.60; N, 8.66.

Found: C, 59.12; H, 5.63; N, 8.57.

MS (EI): 369 (M^+).

^1H -NMR (400MHz, $\text{DMSO}-d_6$) δ (ppm): 0.93 (3H, t, J=7.3Hz),
15 1.02 (3H, t, J=6.8Hz), 1.60 (2H, q, J=7.3Hz), 2.64-2.68 (2H, m),
3.50 (2H, br. s), 3.86 (2H, q, J=7.3Hz), 4.14 (4H, s), 4.99 (1H, s),
6.26 (2H, s), 6.54 (1H, s), 6.57 (1H, d, J=7.8Hz), 6.65 (1H, d, J=7.8Hz),
7.21 (1H, s), 11.97 (1H, br. s).

IR (KBr): ν =3211, 2694, 2878, 2658, 1697, 1506, 1466, 1363, 1302, 1082 cm^{-1} .

20 **Example 81**

Ethyl 4-(benzo[b]furan-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from benzo[b]furan-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
25 same manner as in Example 25.

MP: 123-125°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{21}\text{N}_3\text{O}_3\text{C}_4\text{H}_4\text{O}_4 \cdot 1/2 \text{H}_2\text{O}$: C, 61.19; H, 5.43; N, 8.92.

Found: C, 61.02; H, 5.41; N, 9.27.

MS (EI): 351 (M^+).

30 ^1H -NMR (400MHz, $\text{DMSO}-d_6$) δ (ppm): 0.96 (3H, t, J=7.3Hz),
1.02 (3H, t, J=6.8Hz), 1.63 (2H, q, J=7.3Hz), 2.73-2.76 (2H, m),
3.50 (3H, br. s), 3.93 (2H, q, J=7.3Hz), 5.36 (1H, s), 6.24 (2H, s),
6.43 (1H, s), 7.10-7.21 (2H, m), 7.41-7.48 (3H, m), 9.51 (1H, br. s).

IR (KBr): ν =3190, 3080, 2962, 1705, 1581, 1454, 1359, 1195, 883 cm^{-1} .

Example 82

Ethyl 4-(2-chlorophenyl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate in the same manner as in Example 1.

MP: 213°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{18}\text{ClN}_3\text{O}_2$: C, 61.54; H, 5.47; N, 12.66.

10 Found: C, 61.54; H, 5.46; N, 12.68.

MS (EI): 331 (M^+).

^1H -NMR (400MHz, DMSO-d_6) δ (ppm): 0.85 (3H, t, $J=7.3\text{Hz}$),
1.21 (3H, t, $J=7.3\text{Hz}$), 2.78-2.84 (2H, m), 3.78 (2H, q, $J=7.3\text{Hz}$),
5.58 (1H, s), 7.07-7.12 (2H, m), 7.18 (1H, dd, $J=7.3\text{Hz}$ and
15 7.4Hz), 7.25 (1H, s), 7.34 (1H, d, $J=7.3\text{Hz}$), 9.52 (1H, br. s),
11.97 (1H, br. s).

Example 83

Ethyl 6-butyl-4-(2-chlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP: 209°C.

Anal. Calcd. for: $\text{C}_{19}\text{H}_{22}\text{ClN}_3\text{O}_2 \cdot 1/5 \text{H}_2\text{O}$: C, 62.79; H, 6.21; N, 11.56.

25 Found: C, 62.78; H, 6.11; N, 11.45.

MS (EI): 359 (M^+).

^1H -NMR (400MHz, DMSO-d_6) δ (ppm): 0.85 (3H, t, $J=7.3\text{Hz}$),
0.92 (3H, t, $J=7.3\text{Hz}$), 1.36-1.42 (2H, m), 1.60-1.64 (2H, m), 2.72-
2.76 (1H, m), 2.83-2.86 (1H, m), 3.78 (2H, q, $J=7.3\text{Hz}$), 5.58 (1H, s),
30 7.07-7.11 (2H, m), 7.18 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz), 7.24 (1H, s),
7.34 (1H, d, $J=7.3\text{Hz}$), 9.49 (1H, br. s), 11.96 (1H, br. s).

Example 84

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-methoxymethyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl 4-methoxyacetoacetate in the same manner as in Example 1.

5 MP:160°C.

Anal. Calcd. for: $C_{16}H_{16}ClN_3O_3$: C, 57.33; H, 4.83; N, 12.59.

Found: C, 57.53; H, 4.86; N, 12.58.

MS (EI): 333 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.36 (3H, s), 3.38 (3H, s),
10 4.67 (2H, s), 5.58 (1H, s), 7.08-7.13 (2H, m), 7.19 (1H, dd, J=7.3Hz
and 7.4Hz), 7.32-7.36 (2H, m), 9.14 (1H, br.s), 12.08 (1H, br.s).

Example 85

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl benzoylacetoacetate in the same manner as in Example 1.

MP:214°C.

Anal. Calcd. for: $C_{21}H_{18}ClN_3O_2 \cdot 3/10 H_2O$: C, 65.47; H, 4.87; N, 10.91.

20 Found: C, 65.29; H, 4.73; N, 10.93.

MS (EI): 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.57 (3H, t, J=7.3Hz),
3.52 (2H, q, J=7.3Hz), 5.65 (1H, s), 7.14 (1H, dd, J=7.3Hz and 7.4Hz),
7.27 (1H, dd, J=7.3Hz and 7.4Hz), 7.37-7.40 (8H, m), 9.53 (1H, br.s),
25 12.04 (1H, br.s).

Example 86

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl (4-methoxybenzoyl)acetate in the same manner as in Example 1.

MP:211°C.

Anal. Calcd. for: $C_{22}H_{20}ClN_3O_3$: C, 64.47; H, 4.92; N, 10.25.

Found: C, 64.30; H, 5.00; N, 10.24.

MS (EI): 409 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.64 (3H, t, $J=7.3\text{Hz}$),
3.56 (2H, q, $J=7.3\text{Hz}$), 3.79 (3H, s), 5.63 (1H, s), 6.95 (2H, d, $J=7.3\text{Hz}$),
5 7.13 (1H, dd, $J=7.3\text{Hz}$ and 7.4Hz), 7.24-7.38 (6H, m), 9.45 (1H, br.s),
12.03 (1H, br.s).

Example 87

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

10 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl (thiophen-2-carbonyl)acetate in the same manner as in Example 1.

MP: 200°C.

Anal. Calcd. for: $\text{C}_{19}\text{H}_{16}\text{ClN}_3\text{O}_2\text{S}$: C, 59.14; H, 4.18; N, 10.89.

15 Found: C, 59.04; H, 4.31; N, 11.14.

MS (EI): 385 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.02 (3H, t, $J=7.3\text{Hz}$),
4.04 (2H, q, $J=7.3\text{Hz}$), 5.16 (1H, s), 6.58 (1H, d, $J=7.3\text{Hz}$), 7.18-
7.70 (7H, m), 9.60 (1H, br.s), 12.74 (1H, br.s).

20 Example 88

Ethyl 6-benzyl-4-(2-chlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4-phenylacetoacetate in the same manner as in Example 1.

MP: 247°C.

Anal. Calcd. for: $\text{C}_{22}\text{H}_{20}\text{ClN}_3\text{O}_2\text{O } 1/5 \text{ H}_2\text{O}$: C, 66.48; H, 5.17; N, 10.57.

Found: C, 66.30; H, 5.17; N, 10.37.

MS (EI): 393 (M^+).

30 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.81 (3H, t, $J=7.3\text{Hz}$),
3.76 (2H, q, $J=7.3\text{Hz}$), 4.25 (2H, s), 5.65 (1H, s), 7.06-7.41 (10H, m),
9.68 (1H, br.s), 12.01 (1H, br.s).

Example 89

Ethyl 6-ethyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate in the same manner as in Example 1.

MP:169°C.

Anal. Calcd. for: $C_{18}H_{21}N_3O_3 \cdot 3/10 H_2O$: C, 64.97; H, 6.54; N, 12.63.

Found: C, 64.86; H, 6.84; N, 12.33.

MS (EI): 327 (M^+).

¹H-NMR (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, J=7.3Hz), 1.18 (3H, t, J=7.3Hz), 2.73-2.76 (1H, m), 2.81-2.85 (1H, m), 3.74 (2H, q, J=7.3Hz), 3.85 (3H, s), 5.46 (1H, s), 6.76 (1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94 (2H, m), 7.04 (1H, dd, J=7.3Hz and 7.4Hz), 7.14 (1H, s), 9.32 (1H, br.s), 11.82 (1H, br.s).

Example 90

Ethyl 6-butyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:190°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_3 \cdot 1/2 H_2O$: C, 65.91; H, 7.19; N, 11.53.

Found: C, 65.92; H, 7.07; N, 11.88.

MS (EI): 355 (M^+).

¹H-NMR (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, J=7.3Hz), 0.93 (3H, t, J=7.3Hz), 1.38-1.44 (2H, m), 1.59-1.64 (2H, m), 2.64-2.68 (1H, m), 2.85-2.90 (1H, m), 3.81 (2H, q, J=7.3Hz), 3.85 (3H, s), 5.47 (1H, s), 6.76 (1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94 (2H, m), 7.04 (1H, dd, J=7.3Hz and 7.4Hz), 7.14 (1H, s), 9.29 (1H, br.s), 11.82 (1H, br.s).

Example 91

Methyl 4,7-dihydro-6-methoxymethyl-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and methyl 4-methoxyacetoacetate in the same manner as in Example 1.
MP:186°C.

5 Anal. Calcd. for: $C_{17}H_{19}N_3O_4 \cdot 1/5 H_2O$: C, 61.32; H, 5.87; N, 12.62.
Found: C, 61.34; H, 5.84; N, 12.52.
MS (EI): 329 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.36 (3H, s), 3.38 (3H, s),
3.86 (3H, s), 4.68 (2H, s), 5.46 (1H, s), 6.77 (1H, dd, J=7.3Hz and
10 7.4Hz), 6.90-6.94 (2H, m), 7.06 (1H, dd, J=7.3Hz and 7.4Hz),
7.22 (1H, s), 8.94 (1H, br. s), 11.94 (1H, br. s).

Example 92

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.
MP:195°C.

Anal. Calcd. for: $C_{22}H_{21}N_3O_3$: C, 70.38; H, 5.64; N, 11.19.
20 Found: C, 70.41; H, 5.71; N, 11.27.
MS (EI): 375 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.55 (3H, t, J=7.3Hz),
3.53 (2H, q, J=7.3Hz), 3.88 (3H, s), 5.52 (1H, s), 6.84 (1H, dd, J=7.3Hz
and 7.4Hz), 6.94 (1H, d, J=7.3Hz), 7.09 (1H, dd, J=7.3Hz and 7.4Hz),
25 7.18 (1H, d, J=7.3Hz), 7.23 (1H, s), 7.37-7.40 (5H, m), 9.33 (1H, br. s),
11.90 (1H, br. s).

Example 93

4-(2-Chlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

30 To an aqueous solution (50 mL) of nitromethane (50 g) was added an aqueous solution (50 mL) of n-butylaldehyde (59 g), and the mixture was stirred with heating at 60°C for 6 hours. The reaction mixture was allowed to cool to ambient

temperature, and extracted with ethyl acetate. The solvent was evaporated under reduced pressure to give a brown oil (58 g). To a mixed solution of the obtained oil (50 g) in water (50 mL) and acetone (50 mL) was added sodium chromate (70 g).
5 Under ice-cooling, concentrated sulfuric acid (46 mL) was added dropwise and the mixture was stirred for 5 hours. Ice-water (200 mL) was added and the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column
10 chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-nitropentan-2-one (40 g) as a brown oil. A solution of 2-chlorobenzaldehyde (1.8 g), 3-aminopyrazole (1.0 g) and 1-nitropentan-2-one (1.4 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to
15 room temperature, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (680 mg) as yellow crystals. MP:228°C.

20 Anal. Calcd. for: $C_{15}H_{15}ClN_4O_2$: C, 56.52; H, 4.74; N, 17.58.

Found: C, 56.26; H, 4.91; N, 17.64.

MS (EI): 318 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02 (3H, t, $J=7.3$ Hz), 1.70-1.73 (2H, m), 2.89-2.91 (1H, m), 2.99-3.02 (1H, m), 5.90 (1H, s),
25 7.09-7.21 (3H, m), 7.39 (1H, d, $J=7.3$ Hz), 7.44 (1H, s), 10.84 (1H, br.s), 12.43 (1H, br.s).

Example 94

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

30 To a solution of acetonitrile (4.8 g) in THF (150 mL) was added n-BuLi (67 mmol) at -78°C. Further, methyl butanoate (10 g) was added and the mixture was stirred for one hour. After acidification with hydrochloric acid, the mixture was

extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-cyanopentan-2-one (5.5 g) as a colorless oil. A
5 solution of 2-chlorobenzaldehyde (1.9 g), 3-aminopyrazole (1.0 g) and 1-cyanopentan-2-one (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (1.3 g) as
10 colorless crystals.

MP:248°C.

Anal. Calcd. for: $C_{16}H_{15}ClN_4$: C, 64.32; H, 5.06; N, 18.75.

Found: C, 64.49; H, 5.18; N, 18.81.

MS (EI): 298 (M^+).

15 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, $J=7.3$ Hz), 1.64-1.70 (2H, m), 2.38-2.42 (2H, m), 5.36 (1H, s), 7.23-7.26 (3H, m), 7.32 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.42 (1H, d, $J=7.3$ Hz), 9.83 (1H, br.s), 12.15 (1H, br.s).

Example 95

20 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (76 g) in DMSO (100 mL) was added methyl p-anisate (100 g) and the mixture was stirred with heating at 60°C for one hour. The reaction mixture was
25 allowed to cool, and cold water (500 mL) was added dropwise. The mixture was acidified with hydrochloric acid and the precipitated crystals were collected by filtration. The obtained crystals were extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was
30 recrystallized from ethyl acetate to give benzoylacetonitrile (60 g) as colorless crystals. A solution of 2-chlorobenzaldehyde (1.7 g), 3-aminopyrazole (1.0 g) and benzoylacetonitrile (1.8 g) in acetonitrile (20 mL) was heated

under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (2.63 g) as colorless crystals.

5 MP:124°C.

Anal. Calcd. for: $C_{20}H_{15}ClN_4O \cdot 8/5 H_2O$: C, 61.34; H, 4.68; N, 14.31.

Found: C, 61.32; H, 4.88; N, 14.31.

MS (EI): 362 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.81 (3H, s), 5.48 (1H, s),
10 7.04 (2H, d, $J=7.3$ Hz), 7.26 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.32 (1H, s),
7.35-7.39 (4H, m), 7.45 (1H, d, $J=7.3$ Hz), 9.99 (1H, br. s),
12.22 (1H, br. s).

Example 96

4-(2-Chlorophenyl)-2,4,7,8-tetrahydrofurano[3,4-
15 b]pyrazolo[4,3-e]pyridin-5-one

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4-chloroacetoacetate in the same manner as in Example 1.

MP: >270°C.

20 Anal. Calcd. for: $C_{14}H_{10}ClN_3O_2 \cdot 2/5 H_2O$: C, 57.02; H, 3.69; N, 14.25.

Found: C, 57.13; H, 3.39; N, 14.38.

MS (FAB): 288 (M^++1).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 4.91 (2H, dd, $J=5.6$ Hz and 26.6Hz),
5.34 (1H, s), 7.15-7.24 (3H, m), 7.34 (1H, s), 7.41 (1H, d, $J=6.8$ Hz),
25 10.31 (1H, br. s), 12.20 (1H, br. s).

IR (KBr): $\nu=3167, 2966, 1722, 1637, 1608, 1510, 1026 cm^{-1}$.

Example 97

5'-Ethoxycarbonyl-4',7'-dihydro-6'-propyl-
spiro[benzo[b]thiophene-3(2H),4'-2'H-pyrazolo[3,4-b]pyridine]-
30 5-oxide

A solution of 2-methylthiobenzaldehyde (62 g), Meldrum's acid (58.7 g), ethyl 3-ketohexanoate (64.4 g) and ammonium acetate (40 g) in acetic acid (400 mL) was heated under reflux

overnight. After the solution was cooled to room temperature, the solvent was evaporated under reduced pressure to give colorless crystals (40.2 g). To a solution of dimethylformamide (26.3 g) in chloroform (100 mL) were added, 5 under ice-cooling, phosphorus oxychloride (33.6 mL) and a solution of the obtained colorless crystals (30 g) in chloroform (200 mL), and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (370 g) solution was added and the mixture was stirred for one hour. The 10 reaction mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals. To a solution of the obtained crystals in acetone (500 mL) was 15 added diammonium cerium nitrate (42 g) and the mixture was stirred for 30 minutes. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate. The solvent was evaporated under reduced pressure to give colorless crystals. To a solution of the obtained 20 colorless crystals in tetrahydrofuran (500 mL) was added metachloroperbenzoic acid (12 g) at -78°C and the mixture was stirred for 30 minutes. An aqueous sodium thiosulfate solution was added, and the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give 25 colorless crystals. By recrystallization from ethyl acetate, colorless crystals (15 g) were obtained. To a solution of the obtained colorless crystals in tetrahydrofuran (100 mL) was added lithium diisopropylamide (2.5 eq.) at -78°C . Immediately thereafter, methanol and an aqueous ammonium chloride solution 30 were added. The mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. To a solution of the obtained oil in pyridine (50 mL) was added hydrazine (4.2 g) and the mixture was stirred with

heating for 2 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give title compound (0.8 g) as colorless crystals.

MP: 246°C.

Anal. Calcd. for: $C_{19}H_{21}N_3O_3S$: C, 61.44; H, 5.70; N, 11.31.

Found: C, 61.58; H, 5.81; N, 11.16.

MS (EI): 371 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.70 (3H, t, $J=7.3$ Hz),
0.96 (3H, t, $J=7.3$ Hz), 1.63-1.68 (2H, m), 2.67-2.76 (2H, m),
3.07 (1H, d, $J=14.9$ Hz), 3.64 (2H, q, $J=7.3$ Hz), 4.00 (1H, d, $J=14.9$ Hz),
7.05-7.09 (2H, m), 7.40 (1H, dd, $J=7.3$ Hz and 7.4Hz),
7.50 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.81 (1H, d, $J=7.3$ Hz),
9.83 (1H, br.s), 12.11 (1H, br.s).

Example 98

Ethyl 4,7-dihydro-4-(2-hydroxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of 2-methoxybenzaldehyde (15 g), Meldrum's acid (16 g), ethyl 3-ketohexanoate (17.4 g) and ammonium acetate (9.4 g) in acetic acid (110 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give colorless crystals (8.0 g). To a solution of the obtained colorless crystals (5.2 g) in dichloromethane (150 mL) were added ethanedithiol (20 mL) and aluminum chloride (32 g), and the mixture was stirred for 2 hours. After neutralization with 1N aqueous sodium hydroxide solution, the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals (2.0 g). To a solution of dimethylformamide (1.9 g) in chloroform (10

mL) were added phosphorus oxychloride (2.5 mL) and a solution of the obtained crystals in chloroform (20 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (27 g) solution was added
5 and the mixture was stirred for one hour. The mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give a colorless oil (1.4 g). To a solution
10 of the obtained oil in pyridine (10 mL) was added hydrazine (0.7 g), and the mixture was stirred with heating for 2 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column
15 chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (0.2 g) as colorless crystals.

MP: 177°C

Anal. Calcd. for: $C_{18}H_{21}N_3O_3$: C, 66.04; H, 6.47; N, 12.84.

Found: C, 65.96; H, 6.21; N, 12.66.

20 MS (EI): 327 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.80 (3H, t, $J=7.3$ Hz),
0.96 (3H, t, $J=7.3$ Hz), 1.56-1.59 (2H, m), 2.70-2.80 (2H, m),
3.76 (2H, q, $J=7.3$ Hz), 5.50 (1H, s), 7.28-7.33 (3H, m),
7.63 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.76 (1H, d, $J=7.3$ Hz),
25 9.64 (1H, br.s), 9.68 (1H, br.s), 10.12 (1H, br.s).

Example 99

Ethyl 4-(2-aminophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of ethyl 4,7-dihydro-4-(2-nitrophenyl)-6-
30 propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (1.68 g) in methanol (30 mL) was added 5% palladium-carbon (500 mg), and the mixture was stirred under 10 atm for 3 hours. After removing palladium-carbon by Celite filtration, the solvent

was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (120 mg) as colorless crystals.

5 MP:179°C.

Anal. Calcd. for: $C_{18}H_{22}N_4O_2$: C, 66.24; H, 6.79; N, 17.17.

Found: C, 65.96; H, 6.62; N, 17.16.

MS (EI): 326 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82 (3H, t, $J=7.3$ Hz),
10 0.98 (3H, t, $J=7.3$ Hz), 1.58-1.64 (2H, m), 2.72-2.78 (2H, m),
3.78 (2H, q, $J=7.3$ Hz), 5.52 (1H, s), 6.35-6.38 (2H, br.s), 7.28-
7.36 (3H, m), 7.58 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.78 (1H, d, $J=7.3$ Hz),
9.58 (1H, br.s), 11.48 (1H, br.s).

Example 100

15 Ethyl 4-(2-ethylphenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-ethylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

20 MP:186°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_2 \cdot 1/5 H_2O$: C, 70.03; H, 7.46; N, 12.25.

Found: C, 69.91; H, 7.53; N, 11.98.

MS (EI): 339 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.86 (3H, t, $J=7.3$ Hz),
25 0.94 (3H, t, $J=7.3$ Hz), 1.24 (3H, t, $J=7.3$ Hz), 1.64 (2H, q, $J=7.3$ Hz),
2.64-2.68 (1H, m), 2.77-2.86 (3H, m), 3.78 (2H, q, $J=7.3$ Hz),
5.34 (1H, s), 6.98-7.01 (3H, m), 7.07-7.10 (2H, m), 9.34 (1H, s),
11.89 (1H, s).

Example 101

30 Ethyl 4,7-dihydro-6-propyl-4-(2-propylphenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-propylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate

in the same manner as in Example 25.

MP:197°C.

Anal. Calcd. for: $C_{21}H_{27}N_3O_2$: C, 71.36; H, 7.70; N, 11.89.

Found: C, 71.07; H, 7.73; N, 11.84.

5 MS (EI): 353 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, $J=7.3$ Hz), 0.94-1.00 (6H, m), 1.64 (2H, q, $J=7.3$ Hz), 2.68-2.80 (4H, m), 3.79 (2H, q, $J=7.3$ Hz), 5.33 (1H, s), 6.98-7.06 (5H, m), 9.34 (1H, s), 11.88 (1H, s).

10 **Example 102**

Ethyl 4-(2-butylphenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-butylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner

15 as in Example 25.

MP:175°C.

Anal. Calcd. for: $C_{22}H_{29}N_3O_2$: C, 71.90; H, 7.95; N, 11.43.

Found: C, 71.50; H, 7.94; N, 11.36.

MS (EI): 367 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, $J=7.3$ Hz), 0.92-0.97 (6H, m), 1.40 (2H, q, $J=7.3$ Hz), 1.60-1.66 (4H, m), 2.70-2.82 (4H, m), 3.80 (2H, q, $J=7.3$ Hz), 5.33 (1H, s), 6.97-7.06 (5H, m), 9.34 (1H, s), 11.88 (1H, s).

Example 103

25 Ethyl 4,7-dihydro-4-(indan-4-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from indan-4-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 1.

30 MP:181-183°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_2$: C, 71.77; H, 7.17; N, 11.96.

Found: C, 71.66; H, 7.14; N, 11.88.

MS (EI): 351 (M^+).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90 (3H, t, J=7.3Hz),
0.90 (3H, t, J=7.3Hz), 1.62 (2H, m), 1.80-2.10 (2H, m), 2.52-
3.10 (6H, m), 3.77 (2H, q, J=7.3Hz), 5.17 (1H, s),
6.81 (1H, d, J=6.8Hz), 6.91-6.96 (2H, m), 7.14 (1H, s), 9.33 (1H, br. s),
5 11.87 (1H, br. s).

Example 104

Ethyl 4,7-dihydro-6-propyl-4-(1,2,3,4-tetrahydronaphthalen-5-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Example 105

10 Ethyl 4-(benzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Example 106

Ethyl 4-(benzo[b]thiophen-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from benzo[b]thiophene-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:166°C.

Anal. Calcd. for: C₂₀H₂₁N₃O₂S 2H₂O: C, 59.53; H, 6.25; N, 10.41.

20 Found: C, 59.77; H, 6.46; N, 9.95.

MS (EI): 367 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.74 (3, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 1.65-1.69 (2H, m), 2.70-2.80 (2H, m),
3.71 (2H, q, J=7.3Hz), 5.48 (1H, s), 7.11-7.13 (2H, m),
25 7.26 (1H, dd, J=7.4Hz and 7.5Hz), 7.39 (1H, d, J=5.4Hz),
7.63 (1H, d, J=7.3Hz), 7.68 (1H, d, J=5.4Hz), 9.57 (1H, s),
11.91 (1H, s).

Example 107

5'-Ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H),4'-2'H-pyrazolo[3,4-b]pyridine]

To a solution of 5'-ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H), 4'-2'H-pyrazolo[3,4-b]pyridine]-1-oxide (100 mg) in carbon tetrachloride (20 mL)

was added trimethylsilane iodide (0.1 g), and the mixture was stirred with heating for 30 minutes. The reaction mixture was allowed to cool to ambient temperature, and the mixture was extracted with chloroform. The solvent was evaporated under
5 reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (20 mg) as colorless crystals.

MP:147°C.

10 Anal. Calcd. for: $C_{19}H_{21}N_3O_2S$: C, 64.20; H, 5.95; N, 11.82.

Found: C, 64.18; H, 6.14; N, 11.56.

MS (EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.73 (3H, t, $J=7.3$ Hz),
0.95 (3H, t, $J=7.3$ Hz), 1.64-1.67 (2H, m), 2.56-2.64 (2H, m),
15 3.03 (1H, d, $J=10.2$ Hz), 3.72 (2H, q, $J=7.3$ Hz), 4.03 (1H, d, $J=10.2$ Hz),
6.69 (1H, d, $J=7.3$ Hz), 6.91 (1H, dd, $J=7.3$ Hz and 7.4Hz),
7.03 (1H, dd, $J=7.3$ Hz and 7.4Hz), 7.08 (1H, s), 7.15 (1H, d, $J=7.3$ Hz),
9.65 (1H, br. s), 11.96 (1H, br. s).

Example 108

20 Ethyl 4,7-dihydro-4-methyl-4-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 5'-ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H), 4'-2'H-pyrazolo[3,4-b]pyridin]-1-oxide (100 mg) in tetrahydrofuran (10 mL) were
25 added disodium hydrogenphosphate (1.2 g) and methanol (5 mL) under ice-cooling, and 10% sodium amalgam (3.0 g) was added. The mixture was stirred for 5 hours, filtered through Celite and extracted with chloroform. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was
30 purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (80 mg) as colorless crystals.

MP:207°C.

Anal. Calcd. for: $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91.

Found: C, 69.89; H, 7.18; N, 12.99.

MS (EI): 325 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.71 (3H, t, $J=7.3$ Hz),
5 0.96 (3H, t, $J=7.3$ Hz), 1.64-1.68 (2H, m), 2.28 (3H, s), 2.48-
2.56 (2H, m), 3.71 (2H, q, $J=7.3$ Hz), 6.73-7.01 (5H, m), 7.10 (1H, s),
9.71 (1H, br. s), 11.87 (1H, br. s).

Example 109

Ethyl 4,7-dihydro-6-propyl-4-(2,3,5-trichlorophenyl)-pyrazolo
10 [3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3,5-trichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 218-220°C (decomposition).

15 Anal. Calcd. for: $C_{18}H_{18}Cl_3N_3O_2$: C, 52.13; H, 4.37; N, 10.13.

Found: C, 51.76; H, 4.37; N, 10.07.

MS (EI): 414 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=6.9$ Hz),
0.97 (3H, t, $J=7.3$ Hz), 1.62-1.67 (2H, m), 2.65-2.71 (1H, m), 2.85-
20 2.92 (1H, m), 3.76-3.88 (2H, m), 5.62 (1H, s), 7.03 (1H, d, $J=1.6$ Hz),
7.33 (1H, s), 7.59 (1H, d, $J=2.4$ Hz), 9.69 (1H, s), 12.12 (1H, s).

Example 110

Ethyl 4,7-dihydro-6-propyl-4-(2,3,4,5-
tetrahydrobenzo[b]oxepin-9-yl)-2H-pyrazolo[3,4-b]pyridine-5-
25 carboxylate

Example 111

Ethyl 4-(3-chloro-2-methylphenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-chloro-2-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
30 in the same manner as in Example 1.

MP: 185°C.

Anal. Calcd. for: $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68.

Found: C, 63.37; H, 6.12; N, 11.65.

MS (EI): 359 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.87 (3H, t, J=7.3Hz),
0.95 (3H, t, J=7.3Hz), 1.60-1.66 (2H, m), 2.67-2.69 (1H, m), 2.74-
5 2.78 (1H, m), 3.78 (2H, q, J=7.3Hz), 5.39 (1H, s), 6.95 (1H, d, J=7.3Hz),
7.04 (1H, dd, J=7.3Hz and 7.4Hz), 7.12 (1H, d, J=7.3Hz), 7.24 (1H, s),
9.44 (1H, br.s), 11.94 (1H, br.s).

Example 112

Ethyl 4-(2,1,3-benzothiadiazol-4-yl)-4,7-dihydro-6-propyl-2H-
10 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzothiadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 180°C.

15 Anal. Calcd. for: C₁₈H₁₉N₅O₂S: C, 58.52; H, 5.18; N, 18.96.

Found: C, 58.51; H, 5.19; N, 18.81.

MS (EI): 369 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.62 (3H, t, J=7.3Hz),
1.00 (3H, t, J=7.3Hz), 1.68-1.72 (2H, m), 2.76-2.89 (2H, m),
20 3.72 (2H, q, J=7.3Hz), 6.02 (1H, s), 7.16 (1H, s), 7.20 (1H, d, J=7.3Hz),
7.60 (1H, dd, J=7.3Hz and 7.4Hz), 7.83 (1H, d, J=7.3Hz), 9.55 (1H, s),
11.89 (1H, s).

Example 113

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-methyl-2H-
25 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 25.

MP: 228°C.

30 Anal. Calcd. for: C₁₆H₁₅N₅O₃: C, 59.07; H, 4.65; N, 21.53.

Found: C, 58.85; H, 4.75; N, 21.17.

MS (EI): 325 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.75 (3H, t, J=7.3Hz), 2.42 (3H, s),

3.79 (2H, q, J=7.3Hz), 5.67 (1H, s), 7.14 (1H, d, J=6.6Hz),
7.23 (1H, s), 7.49 (1H, dd, J=9.0Hz and 6.6Hz), 7.78 (1H, d, J=9.0Hz),
9.69 (1H, s), 12.02 (1H, s).

Example 114

5 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-phenyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

10 MP:190°C.

Anal. Calcd. for: C₂₁H₁₇N₅O₃: C, 65.11; H, 4.42; N, 18.08.

Found: C, 64.99; H, 4.59; N, 18.06.

MS (EI): 387 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.54 (3H, t, J=7.3Hz),
15 3.56 (2H, q, J=7.3Hz), 5.68 (1H, s), 7.24 (1H, s), 7.26-7.42 (6H, m),
7.72 (1H, dd, J=7.3Hz and 7.2Hz), 7.94 (1H, d, J=7.3Hz),
9.71 (1H, s), 12.08 (1H, s).

Example 115

20 Ethyl 4-(2,3-dichlorophenyl)-4,7-dihydro-6-phenyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dichlorobenzaldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

MP:214°C.

25 Anal. Calcd. for: C₂₁H₁₇N₅O₃: C, 65.11; H, 4.42; N, 18.08.

Found: C, 64.85; H, 4.48; N, 17.92.

MS (EI): 387 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.57 (3H, t, J=7.3Hz),
3.52 (2H, q, J=7.3Hz), 5.70 (1H, s), 7.30-7.40 (9H, m), 9.61 (1H, s),
30 12.12 (1H, s).

Example 116

(+)Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The compound described in Example 76 was separated using a semi-preparative column for optical resolution (CHIRALPAK AS, 1.0 cm×25 cm, eluent n-hexane/2-propanol/diethylamine=90/10/0.1, flow rate 2.0 mL/min, UV 254 nm, retention time 40 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.) to give the title compound as colorless crystals.
MP: 159°C.
MS(EI): 353 (M⁺).
Specific rotation: $[\alpha]_D^{25} = +260^\circ$ (EtOH, c=0.5).

10 **Example 117**

(-)-Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The compound described in Example 76 was separated using a semi-preparative column for optical resolution (CHIRALPAK AS, 1.0 cm×25 cm, eluent n-hexane/2-propanol/diethylamine=90/10/0.1, flow rate 2.0 mL/min, UV 254 nm, retention time 55 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.) to give the title compound as colorless crystals.
MP: 160°C.
20 MS(EI): 353 (M⁺).
Specific rotation: $[\alpha]_D^{25} = -277^\circ$ (EtOH, c=0.5).

Example 118

4-(2-Bromophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from n-butylaldehyde, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP: 226°C.

Anal. Calcd. for: C₁₅H₁₅BrN₄O₂: C, 49.60; H, 4.16; N, 15.43.

30 Found: C, 49.57; H, 4.28; N, 14.96.

MS(EI): 363 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.02 (3H, t, J=7.3Hz), 1.72-1.76 (2H, m), 2.85-3.05 (2H, m), 5.89 (1H, s), 7.07-7.1 (2H, m),

7.25(1H,dd,J=7.5Hz and 7.4Hz), 7.47(1H,s), 7.56(1H,d,J=7.3Hz),
10.84(1H,s), 12.43(1H,s).

Example 119

4,7-Dihydro-4-(2-methoxyphenyl)-5-nitro-6-propyl-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:223°C.

10 Anal. Calcd. for: C₁₆H₁₈N₄O₃: C, 61.13; H, 5.77; N, 17.82.

Found: C, 61.01; H, 5.87; N, 17.92.

MS(EI): 314(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.03(3H,t,J=7.3Hz), 1.72-
1.78(2H,m), 2.82-3.04(2H,m), 3.86(3H,s), 5.76(1H,s),
15 6.78(1H,dd,J=7.5Hz and 7.4Hz), 6.90(1H,d,J=7.3Hz),
6.95(1H,d,J=7.3Hz), 7.10(1H,dd,J=7.5Hz and 7.4Hz), 7.33(1H,s),
10.68(1H,s), 12.29(1H,s).

Example 120

4,7-Dihydro-4-(2-methylthiophenyl)-5-nitro-6-propyl-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:211°C.

25 Anal. Calcd. for: C₁₆H₁₈N₄O₂S: C, 58.16; H, 5.49; N, 16.96.

Found: C, 57.94; H, 5.47; N, 16.53.

MS(EI): 330(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H,t,J=7.3z), 1.71-
1.76(2H,m), 2.8-3.00(2H,m), 5.89(1H,s), 6.98(1H,d,J=7.3Hz),
30 7.03(1H,dd,J=7.5Hz and 7.4Hz), 7.13(1H,dd,J=7.5Hz and 7.4Hz),
7.28(1H,d,J=7.3Hz), 7.41(1H,s), 10.74(1H,s), 12.34(1H,s).

Example 121

4,7-Dihydro-5-nitro-4-(2-nitrophenyl)-6-propyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

5 MP:204°C.

Anal. Calcd. for: C₁₅H₁₅N₅O₄: C, 54.71; H, 4.59; N, 21.27.

Found: C, 54.50; H, 4.77; N, 21.32.

MS (EI): 329 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.01 (3H, t, J=7.3Hz), 1.69-
10 1.74 (2H, m), 2.85-2.99 (2H, m), 5.67 (1H, s), 6.94 (1H, d, J=7.3Hz),
6.98-7.03 (2H, m), 7.09 (1H, d, J=7.3Hz), 7.38 (1H, s), 10.69 (1H, s),
12.34 (1H, s).

Example 122

4-(2,3-Dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:239°C.

20 Anal. Calcd. for: C₁₅H₁₄Cl₂N₄O₂: C, 51.01; H, 4.00; N, 15.86.

Found: C, 50.70; H, 4.06; N, 15.60.

MS (EI): 353 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02 (3H, t, J=7.3Hz), 1.70-
1.74 (2H, m), 2.89-2.92 (1H, m), 2.96-3.02 (1H, m), 5.96 (1H, s),
25 7.09 (1H, d, J=7.3Hz), 7.24 (1H, dd, J=7.5Hz and 7.4Hz),
7.43 (1H, d, J=7.3Hz), 7.49 (1H, s), 10.98 (1H, s), 12.49 (1H, s).

Example 123

4,7-Dihydro-4-(naphthalen-1-yl)-5-nitro-6-propyl-2H-

pyrazolo[3,4-b]pyridine

30 The title compound was prepared from n-butylaldehyde, naphthalen-1-aldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:226°C.

Anal. Calcd. for: $C_{19}H_{18}N_4O_2$: C, 68.25; H, 5.43; N, 16.76.

Found: C, 68.29; H, 5.20; N, 16.67.

MS (EI): 334 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.06 (3H, t, $J=7.3$ Hz), 1.76-
5 1.82 (2H, m), 2.95-3.06 (2H, m), 6.33 (1H, s), 7.18-7.22 (2H, m),
7.36 (1H, dd, $J=7.5$ Hz and 7.4Hz), 7.54 (1H, dd, $J=7.5$ Hz and 7.4Hz),
7.60 (1H, dd, $J=7.5$ Hz and 7.4Hz), 7.71 (1H, d, $J=7.3$ Hz),
7.92 (1H, d, $J=7.3$ Hz), 8.46 (1H, d, $J=7.3$ Hz), 10.80 (1H, s),
12.29 (1H, s).

10 **Example 124**

4,7-Dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 3,4-dihydro-2H-benzopyran-8-aldehyde and 3-aminopyrazole in
15 the same manner as in Example 93.

MP: 234°C.

Anal. Calcd. for: $C_{18}H_{20}N_4O_3$: C, 63.52; H, 5.92; N, 16.46.

Found: C, 63.22; H, 5.94; N, 16.44.

MS (EI): 340 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02 (3H, t, $J=7.3$ Hz), 1.71-
1.77 (2H, m), 1.92-1.95 (2H, m), 2.69-2.73 (2H, m), 2.85-3.02 (2H, m),
4.23-4.28 (2, m), 5.71 (1H, s), 6.61-6.67 (2H, m),
6.80 (1H, d, $J=7.3$ Hz), 7.37 (1H, s), 10.64 (1H, s), 12.28 (1H, s).

Example 125

25 4-(2,3-Dichlorophenyl)-4,7-dihydro-6-methyl-5-nitro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from acetaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

30 MP: >270°C.

Anal. Calcd. for: $C_{13}H_{10}Cl_2N_4O_2$: C, 48.02; H, 3.10; N, 17.23.

Found: C, 48.05; H, 3.12; N, 17.24.

MS (EI): 325 (M^+).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.66(3H, s), 5.94(1H, s),
7.13(1H, d, J=7.2Hz), 7.22(1H, dd, J=7.3Hz and 7.2Hz),
7.42(1H, d, J=7.3Hz), 7.50(1H, s), 10.94(1H, s), 12.49(1H, s).

Example 126

5 4-(2,3-Dichlorophenyl)-6-ethyl-4,7-dihydro-5-nitro-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from propionaldehyde,
2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 93.

10 MP:250°C.

Anal. Calcd. for: C₁₄H₁₂Cl₂N₄O₂: C, 49.58; H, 3.57; N, 16.52.

Found: C, 49.54; H, 3.62; N, 16.73.

MS (EI): 339 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.29(3H, t, J=7.3Hz), 2.98-
15 3.01(2H, m), 5.94(1H, s), 7.10(1H, d, J=7.3Hz), 7.24(1H, dd, J=7.3Hz
and 7.2Hz), 7.42(1H, d, J=7.2Hz), 7.49(1H, s), 10.93(1H, s),
12.49(1H, s).

Example 127

20 6-Butyl-4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from pentylaldehyde,
2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 93.

MP:220°C.

25 Anal. Calcd. for: C₁₆H₁₆Cl₂N₄O₂: C, 52.33; H, 4.39; N, 15.26.

Found: C, 52.64; H, 4.61; N, 14.51.

MS (EI): 367 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.41-
1.46(2H, m), 1.63-1.68(2H, m), 2.94-3.04(2H, m), 5.95(1H, s),
30 7.08(1H, d, J=7.2Hz), 7.23(1H, dd, J=7.3Hz and 7.2Hz),
7.42(1H, d, J=7.2Hz), 7.48(1H, s), 10.97(1H, s), 12.28(1H, s).

Example 128

4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP:237°C.

Anal. Calcd. for: C₁₆H₁₅BrN₄: C, 55.99; H, 4.41; N, 16.32.

Found: C, 55.97; H, 4.45; N, 16.40.

MS (EI): 343 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.95 (3H, t, J=7.3Hz), 1.64-
10 1.70 (2, m), 2.40-2.44 (2H, m), 5.35 (1H, s), 7.15 (1H, dd, J=7.5Hz and
7.4Hz), 7.22 (1H, d, J=7.3Hz), 7.27 (1H, s), 7.36 (1H, dd, J=7.5Hz and
7.4Hz), 7.59 (1H, d, J=7.3Hz), 9.84 (1H, s), 12.16 (1H, s).

Example 129

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:203°C.

20 Anal. Calcd. for: C₁₇H₁₈N₄O: C, 69.37; H, 6.16; N, 19.03.

Found: C, 69.34; H, 6.25; N, 19.01.

MS (EI): 294 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.96 (3H, t, J=7.3Hz), 1.65-
1.70 (2H, m), 2.38-2.43 (2H, m), 3.83 (3H, s), 5.22 (1H, s),
25 6.89 (1H, dd, J=7.5Hz and 7.4Hz), 6.99 (1H, d, J=7.3Hz),
7.05 (1H, d, J=7.3Hz), 7.15-7.18 (2H, m), 9.65 (1H, s), 12.02 (1H, s).

Example 130

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-propyl-2H-

pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl butanoate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:216°C.

Anal. Calcd. for: $C_{17}H_{18}N_4S$: C, 65.78; H, 5.84; N, 18.05.

Found: C, 65.68; H, 5.81; N, 17.83.

MS (EI): 310 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.96 (3H, t, $J=7.3$ Hz), 1.65-
5 1.70 (2H, m), 2.40-2.46 (2H, m), 2.48 (3H, s), 5.34 (1H, s), 7.13-
7.21 (4H, m), 7.30 (1H, d, $J=7.3$ Hz), 9.75 (1H, s), 12.07 (1H, s).

Example 131

5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-propyl-2H-pyrazolo
[3,4-b]pyridine

10 The title compound was prepared from methyl butanoate,
2-methylbenzaldehyde and 3-aminopyrazole in the same manner as
in Example 94.

MP: 230°C.

Anal. Calcd. for: $C_{17}H_{18}N_4$: C, 73.35; H, 6.52; N, 20.13.

15 Found: C, 73.44; H, 6.61; N, 20.13.

MS (EI): 278 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H, t, $J=7.3$ Hz), 1.65-
1.67 (2H, m), 2.32 (3H, s), 2.35-2.41 (2H, m), 5.13 (1H, s), 7.06-
7.16 (5H, m), 9.69 (1H, s), 12.07 (1H, s).

20 Example 132

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
25 in Example 94.

MP: 216°C.

Anal. Calcd. for: $C_{16}H_{15}N_5O_2$: C, 62.13; H, 4.89; N, 22.64.

Found: C, 62.16; H, 4.93; N, 22.57.

MS (EI): 309 (M^+).

30 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, $J=7.3$ Hz), 1.64-
1.69 (2H, m), 2.36-2.42 (2H, m), 5.38 (1H, s), 7.27 (1H, s), 7.42-
7.49 (2H, m), 7.70 (1H, dd, $J=7.5$ Hz and 7.4Hz), 7.89 (1H, d, $J=7.3$ Hz),
9.91 (1H, s), 12.21 (1H, s).

Example 133

5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
5 2-cyanobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 94.

MP:218°C.

Anal. Calcd. for: C₁₇H₁₅N₅: C, 70.57; H, 5.23; N, 24.21.

Found: C, 70.54; H, 5.30; N, 24.07.

10 MS (EI): 289 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94 (3H, t, J=7.3Hz), 1.63-
1.68 (2H, m), 2.36-2.40 (2H, m), 5.23 (1H, s), 7.26 (1H, s),
7.38 (1H, d, J=7.3Hz), 7.43 (1H, dd, J=7.5Hz and 7.4Hz),
7.69 (1H, dd, J=7.5Hz and 7.4Hz), 7.80 (1H, d, J=7.3Hz), 9.94 (1, s),
15 12.22 (1H, s).

Example 134

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
20 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:242°C.

Anal. Calcd. for: C₁₆H₁₄Cl₂N₄ 1/5 H₂O: C, 57.05; H, 4.31; N, 16.63.

Found: C, 57.23; H, 4.49; N, 16.25.

25 MS (EI): 333 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94 (3H, t, J=7.3Hz), 1.62-
1.68 (2H, m), 2.40-2.46 (2H, m), 5.44 (1H, s), 7.22 (1H, d, J=7.3Hz),
7.30 (1H, s), 7.35 (1H, dd, J=7.5Hz and 7.4Hz), 7.51 (1H, d, J=7.3Hz),
9.89 (1H, s), 12.19 (1H, s).

30 **Example 135**

5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,

naphthalene-1-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:263°C.

Anal. Calcd. for: C₂₀H₁₈N₄: C, 76.41; H, 5.77; N, 17.82.

5 Found: C, 76.05; H, 5.85; N, 17.73.

MS (EI) : 314 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.97 (3H, t, J=7.3Hz), 1.68-1.73 (2H, m), 2.44-2.48 (2H, m), 5.71 (1H, s), 7.04 (1H, s), 7.39-7.46 (4H, m), 7.81 (1H, d, J=7.3Hz), 7.94 (1H, d, J=7.3Hz), 9.83 (1H, s),
10 12.02 (1H, s).

Example 136

5-Cyano-4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
15 3,4-dihydro-2H-benzopyran-8-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:230°C.

Anal. Calcd. for: C₁₉H₂₀N₄O: C, 71.23; H, 6.29; N, 17.49.

Found: C, 71.20; H, 6.48; N, 17.55.

20 MS (EI) : 320 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.95 (3H, t, J=7.3Hz), 1.64-1.70 (2H, m), 1.92-1.95 (2H, m), 2.38-2.43 (2H, m), 2.72-2.76 (2H, m), 4.16-4.27 (2H, m), 5.16 (1H, s), 6.74 (1H, dd, J=7.5Hz and 7.4Hz), 6.83-6.88 (2H, m), 7.20 (1H, s), 9.62 (1H, s), 12.01 (1H, s).

25 Example 137

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the
30 same manner as in Example 94.

MP:194°C.

Anal. Calcd. for: C₁₆H₁₄N₆O: C, 62.73; H, 4.61; N, 27.44.

Found: C, 62.52; H, 4.78; N, 27.19.

MS (EI) : 306 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.92 (3H, t, J=7.3Hz), 1.63-
1.68 (2H, m), 2.38-2.43 (2H, m), 5.40 (1H, s), 7.25 (1H, s),
7.40 (1H, d, J=7.3Hz), 7.58 (1H, dd, J=7.5Hz and 7.4Hz),
5 7.92 (1H, d, J=7.3z), 9.93 (1H, s), 12.13 (1H, s) .

Example 138

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
10 2,1,3-benzothiadiazol-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 94.

MP:195°C.

Anal. Calcd. for: C₁₆H₁₄N₆S: C, 59.61; H, 4.38; N, 26.07.

Found: C, 59.33; H, 4.48; N, 25.76.

15 MS (EI) : 322 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.98 (3H, t, J=7.3Hz), 1.68-
1.74 (2H, m), 2.45-2.50 (2H, m), 5.72 (1H, s), 7.19 (1H, s),
7.43 (1H, d, J=7.3Hz), 7.72 (1H, dd, J=7.5Hz and 7.4Hz),
7.97 (1H, d, J=7.3Hz), 9.87 (1H, s), 12.06 (1H, s) .

20 **Example 139**

5-Cyano-4,7-dihydro-4-(2-methylbenzoxazol-4-yl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-methylbenzoxazole-4-aldehyde and 3-aminopyrazole in the same
25 manner as in Example 94.

MP:208°C.

Anal. Calcd. for: C₁₈H₁₇N₅O 1/5 H₂O: C, 66.94; H, 5.43; N, 21.68.

Found: C, 66.85; H, 5.52; N, 22.09.

MS (EI) : 319 (M⁺) .

30 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.97 (3H, t, J=7.3Hz), 1.67-
1.72 (2H, m), 2.40-2.45 (2H, m), 2.63 (3H, s), 5.51 (1H, s),
7.06 (1H, d, J=7.3Hz), 7.16 (1H, s), 7.29 (1H, dd, J=7.3Hz and 7.2Hz),
7.47 (1H, d, J=7.3Hz), 9.77 (1H, s), 12.06 (1H, s) .

Example 140

R(-) 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of the compound described in Example 137
5 (64.5 g) in THF (1000 mL) was added (-)camphorsulfonic acid
(49 g) at room temperature and the mixture was stirred for 1
hour. The solvent was evaporated under reduced pressure to
give an oil. The obtained oil was recrystallized from
acetonitrile twice to give colorless crystals (11 g). To a
10 solution of the obtained colorless crystals in methanol (50
mL) was added water (50 mL). The mixture was neutralized with
a saturated aqueous sodium hydrogencarbonate solution and
extracted with ethyl acetate. The solvent was evaporated under
reduced pressure. The residual methanol solution was added
15 dropwise to water (1000 mL) and the crystals were collected by
filtration to give the title compound (11 g) as pale-yellow
crystals.

(CHIRALPAK AS, 0.25 cm×25 cm, eluent n-hexane/2-
propanol/diethylamine =80/20/0.1, flow rate 1.5 mL/min, UV 254
20 nm, retention time 10 minutes, DAICEL CHEMICAL INDUSTRIES,
LTD.)

MP: 170°C.

MS(EI): 306(M⁺).

Specific rotation: $[\alpha]_D = -80^\circ$ (EtOH, c=1.0).

25 Example 141

S(+) 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of the compound (54 g), which was
recovered from the mother liquor obtained in Example 140, in
30 THF (600 mL) was added (+)camphorsulfonic acid (41 g) at room
temperature and the mixture was stirred for 1 hour. The
solvent was evaporated under reduced pressure to give an oil.
The obtained oil was recrystallized from acetonitrile twice to

give colorless crystals (12 g). To a solution of the obtained colorless crystals in methanol (50 mL) was added water (50 mL). The mixture was neutralized with a saturated aqueous sodium hydrogencarbonate solution and extracted with ethyl acetate.

5 The solvent was evaporated under reduced pressure and the residual methanol solution was added dropwise to water (1000 mL). The crystals were collected by filtration to give the title compound (11 g) as pale-yellow crystals.

(CHIRALPAK AS, 0.25 cm×25 cm, eluent n-hexane/2-

10 propanol/diethylamine =80/20/0.1, flow rate 1.5 mL/min, UV 254 nm, retention time 13 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.)

MP: 170°C.

MS(EI): 306(M⁺).

15 Specific rotation: $[\alpha]_D^{25} = +82^\circ$ (EtOH, c=1.0).

Example 142

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-
20 chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:158°C.

Anal. Calcd. for: C₁₉H₁₃ClN₄ H₂O: C, 65.05; H, 4.31; N, 15.97.

Found: C, 65.35; H, 4.19; N, 16.21.

25 MS(EI): 332(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.51(1H, s), 7.25-7.51(8H, m), 7.59-7.61(2H, m), 10.07(1H, s), 12.24(1H, s).

Example 143

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine
30

The title compound was prepared from methyl benzoate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:146°C.

Anal. Calcd. for: $C_{20}H_{16}N_4S \cdot 4/5 H_2O$: C, 66.94; H, 4.94; N, 15.61.

Found: C, 66.85; H, 4.81; N, 15.65.

MS (EI): 344 (M^+).

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.48 (3H, s), 5.48 (1H, s), 7.19-7.33 (5H, m), 7.48-7.50 (3H, m), 7.59-7.61 (2H, m), 9.99 (1H, s), 12.16 (1H, s).

Example 144

5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:148°C.

15 Anal. Calcd. for: $C_{20}H_{13}N_5 \cdot 3/5 H_2O$: C, 71.89; H, 4.28; N, 20.96.

Found: C, 71.89; H, 4.33; N, 20.91.

MS (EI): 323 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.38 (1H, s), 7.31 (1H, s), 7.44-7.59 (7H, m), 7.70 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.83 (1H, d, $J=7.3$ Hz),
20 10.21 (1H, s), 12.31 (1H, s).

Example 145

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
25 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:162°C.

Anal. Calcd. for: $C_{19}H_{12}Cl_2N_4$: C, 62.14; H, 3.29; N, 15.26.

Found: C, 61.57; H, 3.93; N, 17.19.

30 MS (EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.59 (1H, s), 7.37-7.42 (3H, m), 7.48-7.55 (4H, m), 7.59-7.62 (2H, m), 10.14 (1H, s), 12.28 (1H, s).

Example 146

5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, naphthalene-1-benzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:174°C.

Anal. Calcd. for: C₂₃H₁₆N₄: C, 79.29; H, 4.63; N, 16.08.

Found: C, 79.50; H, 4.85; N, 16.58.

MS (EI): 348 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 5.87 (1H, s), 7.12 (1H, s), 7.50-7.63 (9H, m), 7.82 (1H, d, J=7.3Hz), 7.96 (1H, d, J=7.3Hz), 8.34 (1H, d, J=7.3Hz), 10.09 (1H, s), 12.12 (1H, s).

Example 147

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>270°C.

Anal. Calcd. for: C₂₀H₁₂BrN₅: C, 59.72; H, 3.01; N, 17.41.

Found: C, 59.53; H, 3.17; N, 17.30.

MS (EI): 402 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 5.63 (1H, s), 7.39 (1H, s), 7.49-7.51 (3H, m), 7.60-7.63 (3H, m), 7.75 (1H, d, J=7.3Hz), 7.85 (1H, d, J=7.3Hz), 10.21 (1H, s), 12.33 (1H, s).

Example 148

5-Cyano-4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 3,4-dihydro-2H-benzopyran-8-benzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:255°C.

Anal. Calcd. for: C₂₂H₁₈N₄O: C, 74.56; H, 5.12; N, 15.81.

Found: C, 74.27; H, 5.11; N, 15.82.

MS (EI) : 354 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.94-1.97 (2H, m), 2.75-2.78 (2H, m),
4.20-4.30 (2H, m), 5.30 (1H, s), 6.80 (1H, dd, J=7.3Hz and 7.2Hz),
5 6.91 (1H, d, J=7.3Hz), 7.02 (1H, d, J=7.3Hz), 7.28 (1H, s), 7.49-
7.51 (3H, m), 7.60-7.63 (2H, m), 9.88 (1H, s), 12.11 (1H, s).

Example 149

5-Cyano-4-(2,3-difluorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl benzoate, 2,3-difluorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 165°C.

Anal. Calcd. for: C₁₉H₁₂F₂N₄ 3/5 H₂O: C, 66.12; H, 3.86; N, 16.23.

15 Found: C, 65.87; H, 3.81; N, 16.46.

MS (EI) : 334 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 5.40 (1H, s), 7.16-7.38 (4H, m),
7.48-7.50 (3H, m), 7.57-7.59 (2H, m), 10.11 (1H, s), 12.30 (1H, s).

Example 150

20 5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

25 MP: 206°C.

Anal. Calcd. for: C₂₀H₁₆N₄O: C, 73.15; H, 4.91; N, 17.06.

Found: C, 73.23; H, 5.14; N, 17.19.

MS (EI) : 328 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 3.86 (3H, s), 5.36 (1H, s),
30 6.94 (1H, dd, J=7.3Hz and 7.2Hz), 7.02 (1H, d, J=7.3Hz), 7.19-
7.25 (3H, m), 7.48-7.51 (3H, m), 7.60-7.63 (2H, m), 9.91 (1H, s),
12.12 (1H, s).

Example 151

5-Cyano-4,7-dihydro-4,6-bis(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
5 as in Example 95.

MP:220°C.

Anal. Calcd. for: C₂₁H₁₈N₄O₂: C, 70.38; H, 5.06; N, 15.63.

Found: C, 69.97; H, 5.13; N, 16.15.

MS(EI): 358 (M⁺).

10 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.86(3H, s), 3.88(3H, s),
5.32(1H, s), 6.95-7.06(3H, m), 7.14-7.25(3H, m),
7.37(1H, d, J=7.3Hz), 7.45(1H, dd, J=7.3Hz and 7.2Hz), 9.74(1H, s),
12.05(1H, s).

Example 152

15 5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(3-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
as in Example 95.

20 MP:192°C.

Anal. Calcd. for: C₂₁H₁₈N₄O₂: C, 70.38; H, 5.06; N, 15.63.

Found: C, 69.97; H, 5.09; N, 15.54.

MS(EI): 358 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H, s), 3.86(3H, s),
25 5.35(1H, s), 6.95(1H, dd, J=7.3Hz and 7.2Hz), 7.01(1H, d, J=7.3Hz),
7.07(1H, d, J=7.3Hz), 7.14(1H, s), 7.18-7.23(5H, m),
7.41(1H, dd, J=7.3Hz and 7.2Hz), 9.88(1H, s), 12.12(1H, s).

Example 153

30 5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
as in Example 95.

MP:149°C.

Anal. Calcd. for: $C_{21}H_{18}N_4O_2 \cdot 1/2 H_2O$: C, 68.65; H, 5.21; N, 15.25.

Found: C, 68.67; H, 4.99; N, 15.35.

MS (EI): 358 (M^+).

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.81 (3H, s), 3.86 (3H, s),
5.33 (1H, s), 6.94 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.01-7.05 (3H, m),
7.18-7.24 (3H, m), 7.56 (2H, d, $J=7.2$ Hz), 9.82 (1H, s), 12.10 (1H, s).

Example 154

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-phenyl-2H-

10 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:221°C.

15 Anal. Calcd. for: $C_{19}H_{13}N_5O_2$: C, 66.47; H, 3.82; N, 20.40.

Found: C, 66.48; H, 4.08; N, 20.41.

MS (EI): 343 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54 (1H, s), 7.34 (1H, s), 7.49-
7.52 (4H, m), 7.59-7.64 (3H, m), 7.74 (1H, dd, $J=7.3$ Hz and 7.2Hz),
20 7.91 (1H, d, $J=7.3$ Hz), 10.16 (1H, s), 12.30 (1H, s).

Example 155

5-Cyano-4,7-dihydro-6-(2-methoxyphenyl)-4-(2-nitrophenyl)-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl o-anisate,
2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 95.

MP:207°C.

Anal. Calcd. for: $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76.

Found: C, 64.03; H, 4.21; N, 18.68.

30 MS (EI): 373 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.85 (3H, s), 5.50 (1H, s),
7.03 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.14 (1H, d, $J=7.3$ Hz), 7.33 (1H, s),
7.37 (1H, d, $J=7.3$ Hz), 7.44-7.52 (2H, m), 7.74-7.80 (2H, m),

7.92 (1H, d, J=7.3Hz), 10.02 (1H, s), 12.25 (1H, s).

Example 156

5-Cyano-4,7-dihydro-6-(3-methoxyphenyl)-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl m-anisate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:220°C.

Anal. Calcd. for: C₂₀H₁₅N₅O₃: C, 64.34; H, 4.05; N, 18.76.

10 Found: C, 63.92; H, 4.14; N, 18.74.

MS (EI): 373 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81 (3H, s), 5.53 (1H, s),
7.07 (1H, d, J=7.3Hz), 7.14-7.18 (2H, m), 7.33 (1H, s),
7.40 (1H, dd, J=7.3Hz and 7.2Hz), 7.50 (1H, dd, J=7.3Hz and 7.2Hz),
15 7.63 (1H, d, J=7.3Hz), 7.74 (1H, dd, J=7.3Hz 7.2Hz),
7.91 (1H, d, J=7.3Hz), 10.13 (1H, s), 12.30 (1H, s).

Example 157

5-Cyano-4,7-dihydro-6-(4-methoxyphenyl)-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl p-anisate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:215°C.

Anal. Calcd. for: C₂₀H₁₅N₅O₃: C, 64.34; H, 4.05; N, 18.76.

25 Found: C, 64.13; H, 4.12; N, 18.69.

MS (EI): 373 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81 (3H, s), 5.51 (1H, s),
7.03 (2H, d, J=7.3Hz), 7.33 (1H, s), 7.47-7.55 (3H, m), 7.61 (1H, d),
7.74 (1H, dd, J=7.3Hz and 7.2Hz), 7.91 (1H, d, J=7.3Hz), 10.07 (1H, s),
30 12.28 (1H, s).

Example 158

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:231°C.

5 Anal. Calcd. for: C₁₉H₁₂N₆O: C, 67.05; H, 3.55; N, 24.69.

Found: C, 66.76; H, 3.90; N, 24.71.

MS (EI) : 340 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.55(1H, s), 7.33(1H, s), 7.50-7.64(7H, m), 7.95(1H, d, J=7.3Hz), 10.20(1H, s), 12.23(1H, s).

10 **Example 159**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
15 same manner as in Example 95.

MP:180°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂: C, 64.86; H, 3.81; N, 22.69.

Found: C, 64.11; H, 3.98; N, 22.34.

MS (EI) : 370 (M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.84(3H, s), 5.56(1H, s), 7.03(1H, dd, J=7.3Hz and 7.2Hz), 7.14(1H, d, J=6.8Hz), 7.33-7.35(2H, m), 7.45(1H, dd, J=7.3Hz and 7.2Hz), 7.54(1H, d, J=7.3Hz), 7.65(1H, dd, J=8.8Hz and 6.8Hz), 7.94(1H, d, J=8.8Hz), 10.04(1H, s), 12.18(1H, s).

25 **Example 160**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
30 same manner as in Example 95.

MP:198°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂ 4/5 H₂O: C, 62.43; H, 4.09; N, 21.84.

Found: C, 62.60; H, 3.99; N, 22.15.

MS (EI) : 370 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 3.80 (3H, s), 5.55 (1H, s), 7.06-7.17 (3H, m), 7.33 (1H, s), 7.40 (1H, dd, J=7.3Hz),
7.52 (1H, d, J=6.6Hz), 7.62 (1H, dd, J=8.8Hz and 6.8Hz),
5 7.95 (1H, d, J=6.8Hz), 10.18 (1H, s), 12.24 (1H, s) .

Example 161

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate,
10 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 244°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂: C, 64.86; H, 3.81; N, 22.69.

Found: C, 64.77; H, 3.91; N, 22.49.

15 MS (EI) : 370 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 3.80 (3H, s), 5.53 (1H, s),
7.02 (2H, d, J=7.3Hz), 7.32 (1H, s), 7.50-7.53 (3H, m),
7.61 (1H, dd, J=8.8Hz and 6.8Hz), 7.94 (1H, d, J=8.8Hz), 10.11 (1H, s),
12.21 (1H, s) .

20 **Example 162**

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the
25 same manner as in Example 95.

MP: 258°C.

MS (EI) : 356 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 5.85 (1H, s), 7.27 (1H, s), 7.51-7.52 (3H, m), 7.61-7.67 (3H, m), 7.76 (1H, dd, J=8.8Hz and 6.8Hz),
30 8.00 (1H, d, J=8.8Hz), 10.13 (1H, s), 12.16 (1H, s) .

Example 163

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:231°C.

5 Anal. Calcd. for: C₂₀H₁₄N₆OS 3/10 H₂O: C, 61.30; H, 3.76; N, 21.45.

Found: C, 61.24; H, 3.74; N, 22.09.

MS (EI): 386 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 3.89 (3H, s), 5.85 (1H, s),
706 (1H, dd, J=7.6Hz and 7.3Hz), 7.17 (1H, d, J=8.3Hz), 7.28 (1H, s),
10 7.43-7.49 (2H, m), 7.69 (1H, d, J=6.8Hz), 7.80 (1H, dd, J=8.8Hz and
6.8Hz), 7.99 (1H, d, J=8.8Hz), 9.97 (1H, s), 12.11 (1H, s).

Example 164

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl m-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:220°C.

Anal. Calcd. for: C₂₀H₁₄N₆OS: C, 62.16; H, 3.65; N, 21.75.

20 Found: C, 61.98; H, 3.70; N, 21.66.

MS (EI): 386 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 3.82 (3H, s), 5.85 (1H, s),
7.08 (1H, d, J=8.3Hz), 7.19 (1H, s), 7.23-7.27 (2H, m),
7.42 (1H, dd, J=7.8Hz and 7.2Hz), 7.61 (1H, d, J=6.6Hz),
25 7.75 (1H, dd, J=8.8Hz and 6.8Hz), 7.99 (1H, d, J=8.1Hz), 10.10 (1H, s),
12.16 (1H, s).

Example 165

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl p-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:238°C.

MS (EI) : 386 (M^+) .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 3.81 (3H, s), 5.83 (1H, s),
7.04 (2H, d, $J=8.8\text{Hz}$), 7.26 (1H, s), 7.73-7.77 (3H, m),
7.75 (1H, dd, $J=8.8\text{Hz}$ and 6.8Hz), 7.99 (1H, d, $J=8.8\text{Hz}$), 10.04 (1H, s),
5 12.14 (1H, s) .

Example 166

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
10 isonicotinate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 236°C.

MS (EI) : 341 (M^+) .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 5.58 (1H, s), 7.35 (1H, s), 7.54-
15 7.64 (4H, m), 7.96 (1H, d, $J=8.1\text{Hz}$), 8.72 (2H, d, $J=5.9\text{Hz}$),
10.40 (1H, s), 12.29 (1H, s) .

Example 167

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl nicotinate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 216°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{11}\text{N}_7\text{O} \cdot 1/5 \text{H}_2\text{O}$: C, 62.68; H, 3.33; N, 28.43.

25 Found: C, 62.73; H, 3.43; N, 28.30.

MS (EI) : 341 (M^+) .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 5.59 (1H, s), 7.35 (1H, s), 7.52-
7.63 (3H, m), 7.95-8.00 (2H, m), 8.69 (1H, d, $J=4.9\text{Hz}$), 8.76 (1H, s),
10.39 (1H, s), 12.28 (1H, s) .

30 **Example 168**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl picolinate,

2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:188°C.

MS (EI) : 341 (M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.59(1H, s), 7.34(1H, s), 7.51-7.53(2H, m), 7.63(1H, dd, J=9.0Hz and 6.6Hz), 7.75(1H, d, J=6.6Hz), 7.95-7.97(2H, m), 8.69(1H, d, J=5.4Hz), 10.20(1H, s), 12.26(1H, s).

Example 169

10 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(naphthalen-1-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-naphthoate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:213°C.

15 Anal. Calcd. for: C₂₃H₁₄N₆O: C, 70.76; H, 3.61; N, 21.53.

Found: C, 70.33; H, 3.74; N, 21.23.

MS (EI) : 390 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.65(1H, s), 7.35-7.66(7H, m), 7.96-8.21(4H, m), 10.35(1H, s), 12.23(1H, s).

20 Example 170

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(furan-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl furan-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:241°C.

Anal. Calcd. for: C₁₇H₁₀N₆O₂: C, 61.82; H, 3.05; N, 25.44.

Found: C, 61.72; H, 3.19; N, 25.34.

MS (EI) : 330 (M⁺).

30 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.54(1H, s), 6.69(1H, s), 7.22(1H, d, J=3.4Hz), 7.32(1H, s), 7.48(1H, d, J=6.3Hz), 7.61(1H, dd, J=9.0Hz and 6.3Hz), 7.89(1H, s), 7.94(1H, d, J=9.0Hz), 10.17(1H, s), 12.26(1H, s).

Example 171

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:230°C.

Anal. Calcd. for: C₁₇H₁₀N₆OS: C, 58.95; H, 2.91; N, 24.26.

Found: C, 58.71; H, 3.08; N, 24.03.

10 MS (EI) : 346 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.54(1H, s), 7.17(1H, dd, J=4.9Hz and 4.8Hz), 7.33(1H, s), 7.49(1H, d, J=6.6Hz), 7.58-7.64(2H, m), 7.77(1H, d, J=4.9Hz), 7.95(1H, d, J=9.0Hz), 10.21(1H, s), 12.27(1H, s).

15 **Example 172**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(naphthalen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-naphthoate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:228°C.

Anal. Calcd. for: C₂₃H₁₄N₆O: C, 70.76; H, 3.61; N, 21.53.

Found: C, 70.66; H, 3.81; N, 20.94.

MS (EI) : 390 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.48(1H, s), 7.24(1H, s), 7.44-7.55(5H, m), 7.85-7.92(4H, m), 8.05(1H, s), 10.21(1H, s), 12.14(1H, s).

Example 173

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(furan-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl furan-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:237°C.

Anal. Calcd. for: $C_{17}H_{10}N_6O_2$: C, 61.82; H, 3.05; N, 25.44.

Found: C, 61.59; H, 3.27; N, 25.01.

MS (EI): 330 (M^+).

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.52 (1H, s), 6.93 (1H, d, $J=1.0$ Hz),
7.31 (1H, s), 7.48 (1H, d, $J=6.6$ Hz), 7.60 (1H, dd, $J=9.0$ Hz and 6.6Hz),
7.80 (1H, dd, $J=1.0$ Hz), 7.94 (1H, d, $J=9.0$ Hz), 8.24 (1H, s),
10.07 (1H, s), 12.25 (1H, s).

Example 174

10 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

15 MP:242°C.

Anal. Calcd. for: $C_{17}H_{10}N_6OS$: C, 58.95; H, 2.91; N, 24.26.

Found: C, 58.52; H, 3.15; N, 23.92.

MS (EI): 346 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54 (1H, s), 7.32 (1H, s),
20 7.42 (1H, d, $J=5.1$ Hz), 7.50 (1H, d, $J=6.6$ Hz), 7.61-7.66 (2H, m),
7.94 (1H, d, $J=9.0$ Hz), 8.00 (1H, s), 10.13 (1H, s), 12.24 (1H, s).

Example 175

6-(Benzo[b]furan-2-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl benzo[b]furan-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>270°C.

Anal. Calcd. for: $C_{21}H_{12}N_6O_2$: C, 66.31; H, 3.18; N, 22.09.

30 Found: C, 66.26; H, 3.34; N, 21.53.

MS (EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.62 (1H, s), 7.31-7.36 (2H, m),
7.45 (1H, dd, $J=9.0$ Hz and 6.7Hz), 7.53 (1H, d, $J=6.7$ Hz), 7.61-

7.65(3H,m), 7.77(1H,d,J=7.3Hz), 7.96(1H,d,J=9.0Hz),
10.44(1H,s), 12.33(1H,s).

Example 176

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-methyl-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl acetate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 94.

MP:212°C.

10 Anal. Calcd. for: C₁₄H₁₀N₆O 3/5 H₂O: C, 58.17; H, 3.91; N, 29.07.

Found: C, 58.45; H, 4.08; N, 28.61.

MS(EI): 278 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.14(3H,s), 5.40(1H,s),
7.25(1H,s), 7.40(1H,d,J=6.6Hz), 7.59(1H,dd,J=9.0Hz 6.6Hz),
15 7.92(1H,d,J=9.0Hz), 9.98(1H,s), 12.13(1H,s).

Example 177

4-(2,1,3-Benzoxadiazol-4-yl)-6-butyl-5-cyano-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pentanoate,
20 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 94.

MP:200°C.

Anal. Calcd. for: C₁₇H₁₆N₆O: C, 63.74; H, 5.03; N, 26.23.

Found: C, 63.85; H, 5.01; N, 26.26.

25 MS(EI): 320 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H,t,J=7.3Hz), 1.30-
1.39(2H,m), 1.57-1.65(2H,m), 2.06-2.40(2H,m), 5.39(1H,s),
7.25(1H,s), 7.39(1H,d,J=6.6Hz), 7.59(1H,dd,J=9.0Hz and 6.6Hz),
7.91(1H,d,J=9.0Hz), 9.94(1H,s), 12.13(1H,s).

30 **Example 178**

Ethyl 4-(2-chloro-3-methylphenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2-chloro-m-xylene (15 ml), N-

bromosuccinimide (23.3 g) and benzoyl peroxide (200 mg) in carbon tetrachloride (150 ml) was heated under reflux for 6 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained
5 residue was purified by silica gel column chromatography (eluent: hexane) to give 2-bromomethyl-1-chloro-6-methylbenzene (16.0 g) as a colorless oil. 2-Bromomethyl-1-chloro-6-methylbenzene (25.4 g) and hexamethylenetetramine (32.4 g) were dissolved in acetic acid-water (1:1, 10 ml) and
10 the mixture was heated under reflux for 5 hours. To the reaction mixture was added concentrated hydrochloric acid (40 ml) and the mixture was heated under reflux for 1 hour. The reaction mixture was extracted with ethyl acetate. The extract was washed with an aqueous sodium hydrogencarbonate solution
15 and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 2-chloro-3-methylbenzaldehyde (19.4 g) as a yellow oil. Subsequently, the title compound was prepared from 2-chloro-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
20 in the same manner as in Example 25.

MP:198-200°C.

Anal. Calcd. for: $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68.

Found: C, 63.19; H, 6.14; N, 11.71.

MS (EI): 359 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, $J=7.3$ Hz), 0.97 (3H, t, $J=7.3$ Hz), 1.65 (2H, m), 2.33 (3H, s), 2.68-2.71 (1H, m), 2.79-2.84 (1H, m), 3.72-3.82 (2H, m), 5.63 (1H, s), 6.93-6.96 (1H, m), 7.05-7.07 (2H, m), 7.24 (1H, s), 9.46 (1H, s), 11.94 (1H, s).

Example 179

30 Ethyl 4-(2-chloro-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-chloro-3-nitrobenzoic acid (5.0 g) in THF (50 ml) was added borane-tetrahydrofuran complex (1M THF

solution, 30 ml) under ice-cooling and the mixture was stirred at room temperature for 24 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract
5 was washed with water and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give a pale-yellow solid (3.7 g). The obtained pale-yellow solid (1.6 g) and manganese dioxide (1.7 g) were heated under reflux in toluene for 4.5 hours. The
10 insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (4:1)) to give 2-chloro-3-nitrobenzaldehyde (1.3 g) as a pale-yellow solid. Subsequently, the title compound
15 was prepared from 2-chloro-3-nitrobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MS(EI): 390 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, $J=6.8\text{Hz}$),
20 0.97 (3H, t, $J=7.3\text{Hz}$), 1.64-1.68 (2H, m), 2.70-2.85 (2H, m), 3.73-3.86 (2H, m), 5.67 (1H, s), 7.31 (1H, s), 7.39-7.47 (2H, m), 7.73 (1H, dd, $J=1.5, 7.8\text{Hz}$), 9.67 (1H, s), 12.10 (1H, s).

Example 180

Ethyl 4-(2-chloro-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-
25 pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-chloro-3-methylbenzaldehyde (19.4 g) in ethanol (45 ml) was added an aqueous hydroxylamine hydrochloride (9.7 g) solution (12 ml), and an aqueous sodium hydroxide (6.9 g) solution (10 ml) was added. The mixture was
30 stirred at room temperature for 1.5 hours. Water (500 ml) was added and the precipitated crystals were collected by filtration. The obtained white crystals (16.1 g) were dissolved in acetic anhydride (50 ml) and the mixture was

heated under reflux for 2.5 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) to give 2-cyano-6-methylchlorobenzene (10.9 g) as a white solid. A suspension of 2-cyano-6-methylchlorobenzene (10.9 g), N-bromosuccinimide (12.8 g) and benzoyl peroxide (523 mg) in carbon tetrachloride (100 ml) was heated under reflux for 3.5 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (20:1)) to give 2-chloro-3-cyanobenzaldehyde (12.8 g) as a colorless oil. Subsequently, the title compound was prepared from 2-chloro-3-cyanobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 213-215°C.

Anal. Calcd. for: $C_{19}H_{19}ClN_4O_2$: C, 61.54; H, 5.16; N, 15.11.

Found: C, 61.25; H, 5.36; N, 14.71.

MS (EI): 370 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.86 (3H, t, $J=6.9$ Hz), 0.96 (3H, t, $J=7.3$ Hz), 1.65 (2H, m), 2.70-2.80 (2H, m), 3.73-3.81 (2H, m), 5.63 (1H, s), 7.31 (1H, s), 7.42-7.44 (2H, m), 7.72 (1H, dd, $J=3.0, 6.4$ Hz), 9.65 (1H, s), 12.08 (1H, s).

IR (KBr): $\nu=3344, 3292, 2985, 2954, 2242, 1652$ cm $^{-1}$.

Example 181

Ethyl 4-(2,3-dibromophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2-bromo-3-nitrotoluene (5.0 g), iron (3.9 g) and ammonium chloride (3.7 g) in ethanol (50 ml)-water (17 ml) was heated under reflux for 2 hours. The insoluble matter was filtered off. To the filtrate was added ethyl acetate (100 ml) and the mixture was washed with water and a saturated aqueous sodium chloride solution, and dried over

anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) to give a pale-yellow oil (4.8 g). The obtained pale-yellow oil (4.8 g) was dissolved in 47% hydrobromic acid (50 ml). Under ice-cooling, an aqueous sodium nitrite (1.6 g) solution (18 ml) was added and the mixture was stirred under ice-cooling for 30 minutes. The reaction mixture was added dropwise to a solution of cuprous bromide (2.0 g) in 47% hydrobromic acid (20 ml) over 30 minutes and the mixture was stirred at 60°C for 4.5 hours. To the reaction mixture was added water (100 ml) and the mixture was extracted with ethyl acetate. The extract was washed with water and a saturated aqueous sodium hydrogencarbonate solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (9:1)) to give 2,3-dibromotoluene (2.6 g) as a brown oil. A suspension of 2,3-dibromotoluene (2.6 g), N-bromosuccinimide (1.85 g) and benzoyl peroxide (50 mg) in carbon tetrachloride (30 ml) was heated under reflux for 2 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane) to give a colorless oil (1.1 g). To a solution of the obtained colorless oil (1.1 g) in dimethyl sulfoxide (8.6 ml) - methylene chloride (2 ml) was added trimethylamine-N-oxide (1.0 g) under ice-cooling and the mixture was stirred at room temperature for 1 hour. The reaction mixture was poured into water (50 ml) and the mixture was extracted with ethyl acetate. The extract was washed with 5% hydrochloric acid, a saturated aqueous sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate.

The solvent was evaporated to give 2,3-dibromobenzaldehyde (0.5 g) as a brown oil. Then the title compound was prepared from 2,3-dibromobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:180-183°C (decomposition).

MS(EI):469(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=7.3Hz),
0.96(3H, t, J=7.3Hz), 1.65(2H, m), 2.70-2.80(2H, m), 3.72-
3.83(2H, m), 5.67(1H, s), 7.07(1H, d, J=5.8Hz),
10 7.18(1H, dd, J=5.8, 7.8Hz), 7.48(1H, d, J=7.8Hz), 9.57(1H, s),
12.02(1H, s).

IR(KBr):ν=3344, 3292, 2985, 2954, 2242, 1652cm⁻¹.

Example 182

Ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 H₂O

A suspension of 2-bromo-3-nitrotoluene (5.1 g), N-bromosuccinimide (4.2 g) and benzoyl peroxide (229 mg) in carbon tetrachloride (50 ml) was heated under reflux for 3 hours. The insoluble material was filtered off and the
20 filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a yellow solid (5.4 g). The obtained yellow solid (5.4 g) and hexamethylenetetramine (5.1 g) were dissolved in acetic acid-
25 water (1:1, 16 ml) and the mixture was heated under reflux for 2 hours. To the reaction mixture was added concentrated hydrochloric acid (6 ml) and the mixture was heated under reflux for 15 minutes. The reaction mixture was extracted with ethyl acetate. The extract was washed with water, an aqueous
30 sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the obtained residue was purified by silica gel column chromatography (eluent:

hexane-ethyl acetate (5:1)) and crystallized (hexane-ethyl acetate (5:1)) to give 2-bromo-3-nitrobenzaldehyde (1.2 g) as yellow crystals. Subsequently, the title compound was prepared from 2-bromo-3-nitrobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:213-215°C.

Anal. Calcd. for: $C_{18}H_{19}BrN_4O_4 \cdot \frac{1}{2} H_2O$: C, 48.66; H, 4.54; N, 12.61.

Found: C, 48.34; H, 4.20; N, 13.04.

MS (EI): 435 (M^+).

¹H-NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, J=7.3Hz), 0.97 (3H, t, J=7.3Hz), 1.63-1.68 (2H, m), 2.77-2.81 (2H, m), 3.72-3.85 (2H, m), 5.68 (1H, s), 7.33-7.36 (2H, m), 7.47 (1H, dd, J=7.8, 7.8Hz), 7.66 (1H, d, J=7.8Hz), 9.67 (1H, s), 12.09 (1H, s).

15 Example 183

Ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromo-m-xylene, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 180.

MP:210-212°C (decomposition).

Anal. Calcd. for: $C_{19}H_{19}BrN_4O_2$: C, 54.95; H, 4.61; N, 13.49.

Found: C, 54.98; H, 4.94; N, 13.11.

MS (EI): 415 (M^+).

¹H-NMR (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H, t, J=6.8Hz), 0.97 (3H, t, J=7.3Hz), 1.62-1.68 (2H, m), 2.75-2.80 (2H, m), 3.72-3.83 (2H, m), 5.63 (1H, s), 7.32 (1H, s), 7.39-7.48 (2H, m), 7.68 (1H, dd, J=1.9, 7.3Hz), 9.65 (1H, s), 12.07 (1H, s).

Example 184

4-(2-Chloro-3-cyanophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-chloro-3-cyanobenzaldehyde and 3-aminopyrazole in the same

manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: $C_{17}H_{14}Cl_3N_5$: C, 63.06; H, 4.36; N, 21.63.

Found: C, 63.10; H, 4.42; N, 21.61.

5 MS (EI): 323 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, $J=7.3$ Hz), 1.61-1.71 (2H, m), 2.35-2.49 (2H, m), 5.47 (1H, s), 7.32 (1H, s), 7.52-7.59 (2H, m), 7.87 (1H, dd, $J=2.0, 7.3$ Hz), 9.95 (1H, s), 12.24 (1H, s).

Example 185

10 4-(2-Chloro-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-chloro-3-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 MP: 234-235°C.

Anal. Calcd. for: $C_{16}H_{14}ClN_5O_2$: C, 55.90; H, 4.10; N, 20.37.

Found: C, 55.93; H, 4.34; N, 20.72.

MS (EI): 343 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, $J=7.3$ Hz), 1.64-1.69 (2H, m), 2.37-2.45 (2H, m), 5.52 (1H, s), 7.34 (1H, s), 7.54-7.60 (2H, m), 7.89 (1H, dd, $J=2.0, 6.9$ Hz), 9.97 (1H, s), 12.25 (1H, s).

Example 186

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine 1/5 H_2O

25 The title compound was prepared from methyl butanoate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 275-279°C (decomposition).

Anal. Calcd. for: $C_{17}H_{14}BrN_5 \cdot 1/5 H_2O$: C, 55.05; H, 3.89; N, 18.88.

30 Found: C, 54.98; H, 3.91; N, 18.81.

MS (EI): 368 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, $J=7.3$ Hz), 1.64-1.69 (2H, m), 2.38-2.43 (2H, m), 5.47 (1H, s), 7.33 (1H, s), 7.54-

7.60 (2H, m), 7.83 (1H, dd, J=2.0, 7.4 Hz), 9.95 (1H, s), 12.24 (1H, s).

Example 187

(+) Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 To a solution of the compound (1.94 g) described in Example 73 in acetonitrile (15 ml) was added (-)-10-camphorsulfonic acid (1.23 g) at 50°C and the mixture was stirred under ice-cooling for 30 minutes. The precipitated crystals were collected by filtration and recrystallized
10 (ethanol-ethyl acetate (2:1), 30 ml) to give white crystals (0.81 g). The obtained white crystals were suspended in water and a saturated aqueous sodium hydrogencarbonate solution was added. The mixture was extracted with ethyl acetate and the extract was washed with water and a saturated aqueous sodium
15 chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give a colorless transparent oil. The obtained colorless transparent oil was crystallized from ethyl acetate to give the title compound (470 mg) as white crystals.

20 MP: 159-161°C.

Anal. Calcd. for: C₂₁H₂₅N₃O₃: C, 68.64; H, 6.86; N, 11.44.

Found: C, 68.37; H, 6.86; N, 11.26.

Specific rotation: $[\alpha]_D^{20} = +200^\circ$ (EtOH, c=0.5).

MS (EI): 367 (M⁺).

25 ¹H-NMR (400 MHz, DMSO-d₆) δ (ppm): 0.91 (3H, t, J=6.8 Hz), 0.98 (3H, t, J=7.3 Hz), 1.60-1.70 (2H, m), 1.90-2.00 (2H, m), 2.67-2.82 (4H, m), 3.81 (2H, m), 4.25 (2H, m), 5.42 (1H, s), 6.62 (1H, dd, J=7.4, 7.8 Hz), 6.72-6.76 (2H, m), 7.18 (1H, s), 9.26 (1H, s), 11.81 (1H, s).

30 Example 188

(-) Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The filtrate obtained by filtering off the (-)-10-

camphorsulfonate salt in Example 187 was concentrated under reduced pressure and suspended in water. To the suspension was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract
5 was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give white crystals (780 mg). By the same process as in Example 187 using the obtained white crystals
10 and (+)-10-camphorsulfonic acid, the title compound (150 mg) was obtained as white crystals.

MP:160-161°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44.

Found: C, 68.49; H, 6.81; N, 11.42.

15 Specific rotation: $[\alpha]_D = -202^\circ$ (EtOH, $c=0.5$)

MS (EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, $J=6.8$ Hz),
0.98 (3H, t, $J=7.3$ Hz), 1.60-1.70 (2H, m), 1.90-2.00 (2H, m), 2.67-
2.82 (4H, m), 3.81 (2H, m), 4.25 (2H, m), 5.42 (1H, s), 6.62 (1H, dd,
20 $J=7.4, 7.8$ Hz), 6.72-6.76 (2H, m), 7.18 (1H, s), 9.26 (1H, s),
11.81 (1H, s).

Example 189

4-(2-Bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl butanoate, 2-bromo-3-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:250-255°C (decomposition).

Anal. Calcd. for: $C_{16}H_{14}BrN_5O_2$: C, 49.50; H, 3.63; N, 18.04.

30 Found: C, 49.37; H, 3.76; N, 18.02.

MS (EI): 388 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, $J=7.6$ Hz), 1.64-
1.70 (2H, m), 2.39-2.44 (2H, m), 5.53 (1H, s), 7.34 (1H, s),

7.49 (1H, d, J=7.8Hz), 7.60 (1H, dd, J=7.8, 8.0Hz),
7.82 (1H, d, J=8.0Hz), 9.97 (1H, s), 12.25 (1H, s).

Example 190

Ethyl 4,7-dihydro-4-(2-methoxy-3-methylphenyl)-6-propyl-2H-
5 pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2,6-dimethylphenol (19.5 g), iodomethane (31 ml) and potassium carbonate (33.2 g) in dimethylformamide (200 ml) was stirred at 60°C for 10 hours. The reaction mixture was poured into water (300 ml) and the mixture was
10 extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane) to give 2-methoxy-m-xylene (12
15 g) as a colorless oil. A suspension of 2-methoxy-m-xylene (5.1 g), N-bromosuccinimide (4.2 g) and benzoyl peroxide (229 mg) in carbon tetrachloride (50 ml) was heated under reflux for 3 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained
20 residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a yellow solid (5.4 g). The obtained yellow solid (5.4 g) and hexamethylenetetramine (5.1 g) were dissolved in acetic acid-water (1:1, 16 ml) and the mixture was heated under reflux for
25 2 hours. To the reaction mixture was added concentrated hydrochloric acid (6 ml) and the mixture was heated under reflux for 15 minutes. The reaction mixture was extracted with ethyl acetate. The extract was washed with water, an aqueous sodium hydrogencarbonate solution and a saturated aqueous
30 sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) and crystallized (hexane-ethyl

acetate (5:1)) to give 2-methoxy-3-methylbenzaldehyde (1.2 g) as yellow crystals. Subsequently, the title compound was prepared from 2-methoxy-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:220-222°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_3$: C, 67.58; H, 7.09; N, 11.82.

Found: C, 67.47; H, 7.02; N, 11.91.

MS (EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.0$ Hz),
10 0.97 (3H, t, $J=7.3$ Hz), 1.60-1.70 (2H, m), 2.23 (3H, s), 2.66-
2.85 (2H, m), 3.81 (3H, s), 3.81-3.85 (2H, m), 5.43 (1H, s), 6.82-
6.91 (3H, m), 7.13 (1H, s), 9.31 (1H, s), 11.82 (1H, s).

Example 191

Ethyl 4-(3-cyano-2-methoxyphenyl)-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxy-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 180.

MP:220-222°C.

20 Anal. Calcd. for: $C_{20}H_{22}N_4O_3$: C, 65.56; H, 6.05; N, 15.29.

Found: C, 65.20; H, 6.10; N, 15.23.

MS (EI): 366 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.1$ Hz),
0.96 (3H, t, $J=7.3$ Hz), 1.60-1.70 (2H, m), 2.70-2.80 (2H, m), 3.75-
25 3.90 (2H, m), 4.02 (3H, s), 5.46 (1H, s), 7.14-7.19 (2H, m),
7.32 (1H, d, $J=6.1$ Hz), 7.53 (1H, d, $J=7.8$ Hz), 9.51 (1H, s),
11.97 (1H, s).

Example 192

5-Cyano-6-ethyl-4,7-dihydro-4-(2-nitrophenyl)-2H-pyrazolo[3,4-
30 b]pyridine

The title compound was prepared from methyl propionate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:228-230°C (decomposition).

Anal. Calcd. for: $C_{15}H_{13}N_5O_2$: C, 61.01; H, 4.44; N, 23.72.

Found: C, 60.72; H, 4.51; N, 23.78.

MS (EI): 295 (M^+).

- 5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.21 (3H, t, $J=7.4$ Hz), 2.42-2.49 (2H, m), 5.37 (1H, s), 7.27 (1H, s), 7.43-7.49 (2H, m), 7.70 (1H, dd, $J=7.6, 8.0$ Hz), 7.89 (1H, d, $J=8.0$ Hz), 9.94 (1H, s), 12.21 (1H, s).

Example 193

- 10 5-Cyano-4-(2,3-dichlorophenyl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2,3-dichlorobenzaldehyde, 3-aminopyrazole and 1-cyanobutan-2-one in the same manner as in Example 94.

- 15 MP: >300°C.

Anal. Calcd. for: $C_{15}H_{12}Cl_2N_4$: C, 56.44; H, 3.79; N, 17.55.

Found: C, 56.33; H, 3.86; N, 17.67.

MS (EI): 319 (M^+).

- 20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.21 (3H, t, $J=7.6$ Hz), 2.38-2.49 (2H, m), 5.43 (1H, s), 7.23 (1H, d, $J=6.8$ Hz), 7.31-7.37 (2H, m), 7.51 (1H, dd, $J=1.7, 8.1$ Hz), 9.92 (1H, s), 12.19 (1H, s).

Example 194

5-Cyano-6-ethyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

- 25 The title compound was prepared from methyl propionate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 230-232°C.

Anal. Calcd. for: $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99.

- 30 Found: C, 68.16; H, 5.97; N, 20.39.

MS (EI): 280 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.22 (3H, t, $J=7.6$ Hz), 2.42-2.49 (2H, m), 3.84 (3H, s), 5.21 (1H, s), 6.86-6.91 (1H, m),

6.99 (1H, d, J=8.3Hz), 7.05 (1H, d, J=7.6Hz), 7.15-7.19 (2H, m),
9.68 (1H, s), 12.02 (1H, s).

Example 195

4-(2-Chloro-3-cyanophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate,
2-chloro-3-cyanobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: >300°C.

10 Anal. Calcd. for: C₁₆H₁₂ClN₅: C, 62.04; H, 3.90; N, 22.61.

Found: C, 61.74; H, 4.14; N, 22.93.

MS (EI): 309 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.21 (3H, t, J=7.6Hz), 2.42-
2.49 (2H, m), 5.45 (1H, s), 7.33 (1H, s), 7.52-7.60 (2H, m), 7.87
15 (1H, dd, J=2.0, 7.3Hz), 9.97 (1H, s), 12.23 (1H, s).

Example 196

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-6-ethyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate,
20 2,1,3-benzoxazole-4-aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 206-208°C (decomposition).

Anal. Calcd. for: C₁₅H₁₂N₆O: C, 61.64; H, 4.14; N, 28.75.

Found: C, 61.43; H, 4.41; N, 28.85.

25 MS (EI): 292 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.20 (3H, t, J=7.6Hz), 2.40-
2.50 (2H, m), 5.40 (1H, s), 7.26 (1H, s), 7.40 (1H, d, J=6.6Hz),
7.58 (1H, dd, J=6.6, 9.0Hz), 7.92 (1H, d, J=9.0Hz), 9.97 (1H, s),
12.14 (1H, s).

30 **Example 197**

4-(2-Chlorophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate,

2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₅H₁₃ClN₄: C, 63.27; H, 4.60; N, 19.68.

5 Found: C, 63.14; H, 4.69; N, 19.67.

MS (EI): 284 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.21 (3H, t, J=7.6Hz), 2.42-2.49 (2H, m), 5.35 (1H, s), 7.22-7.26 (3H, m), 7.30-7.34 (1H, m), 7.42 (1H, d, J=7.8Hz), 9.85 (1H, s), 12.15 (1H, s).

10 Example 198

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same
15 manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₆H₁₂BrN₅: C, 54.25; H, 3.41; N, 19.77.

Found: C, 54.13; H, 3.56; N, 19.98.

MS (EI): 354 (M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.21 (3H, t, J=7.6Hz), 2.43 (2H, m), 5.46 (1H, s), 7.33 (1H, s), 7.56-7.60 (2H, m), 7.82-7.84 (1H, m), 9.98 (1H, s), 12.24 (1H, s).

Example 199

4-(2-Bromophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-
25 b]pyridine

The title compound was prepared from methyl propionate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 250-253°C (decomposition).

30 Anal. Calcd. for: C₁₅H₁₃BrN₄: C, 54.73; H, 3.98; N, 17.02.

Found: C, 54.28; H, 3.96; N, 16.94.

MS (EI): 329 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.21 (3H, t, J=7.6Hz), 2.42-

2.45 (2H, m), 5.34 (1H, s), 7.16 (1H, dd, J=7.5, 7.6 Hz),
7.22 (1H, d, J=6.6 Hz), 7.27 (1H, s), 7.36 (1H, dd, J=6.3, 7.3 Hz),
7.59 (1H, d, J=6.8 Hz), 9.86 (1H, s), 12.15 (1H, s).

Example 200

5 Ethyl 4-(2-chlorophenyl)-6-cyano-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate 1/4 hydrate

A solution of 1,1'-carbonylbis-1H-imidazole (22.5 g),
ethanol (8.1 ml) and toluene (100 ml) was stirred at room
temperature for 1.5 hours. To the reaction mixture was added
10 ice-water (100 ml) and the mixture was extracted with ethyl
acetate. The extract was washed with a saturated aqueous
sodium chloride solution and dried over anhydrous magnesium
sulfate. The solvent was evaporated and the obtained residue
was purified by silica gel column chromatography (eluent:
15 hexane-ethyl acetate (1:1)) to give a colorless oil (19.3 g).
A solution of the obtained residue (19.3 g) and pyruvic
aldehyde dimethyl acetal (11.1 ml) in toluene (50 ml) was
added dropwise to a suspension of sodium hydride (8.44 g) in
toluene (250 ml) under reflux with heating over 15 minutes,
20 and the mixture was heated under reflux for 1.5 hours. To the
reaction mixture was added a 10% aqueous citric acid solution
(610 ml) and the mixture was extracted with ethyl acetate. The
extract was washed with a saturated aqueous sodium chloride
solution and dried over anhydrous magnesium sulfate. The
25 solvent was evaporated and the obtained residue was purified
by silica gel column chromatography (eluent: hexane-ethyl
acetate (5:1)) to give ethyl 4,4-dimethoxy-3-oxobutanoate
(15.1 g) as a colorless oil. Subsequently, ethyl 4-(2-
chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-
30 b]pyridine-5-carboxylate was obtained as a yellow solid from
2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4,4-dimethoxy-
2-oxobutanoate in the same manner as in Example 1. To a
solution of ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-

dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (463 mg) in tetrahydrofuran (5 ml) was added 1N hydrochloric acid (10 ml) and the mixture was stirred at room temperature for 6 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give ethyl 4-(2-chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (290 mg) as a yellow solid. A solution of ethyl 4-(2-chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (290 mg) and hydroxylamine-O-sulfonic acid (128.5 mg) in water (10 ml)-ethanol (10 ml) was stirred at 80°C for 2 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) and crystallized from ethanol-ethyl acetate to give the title compound (53 mg) as yellow crystals.

MP: 275-278°C (decomposition).

Anal. Calcd. for: $C_{16}H_{13}ClN_4O_2 \cdot 1/4 H_2O$: C, 57.66; H, 4.08; N, 16.81.

Found: C, 57.54; H, 4.06; N, 16.66.

MS (EI): 328 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H, t, $J=7.1$ Hz), 3.91 (2H, m), 5.67 (1H, s), 7.15-7.19 (2H, m), 7.25 (1H, dd, $J=7.3, 8.3$ Hz), 7.33 (1H, s), 7.39 (1H, d, $J=8.3$ Hz), 10.81 (1H, s), 12.34 (1H, s).

Example 201

4-(2-Chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-6-

propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP:>250°C.

Anal. Calcd. for: C₁₇H₁₄ClF₃N₄: C, 55.67; H, 3.85; N, 15.28.

Found: C, 55.81; H, 3.97; N, 15.44.

MS (EI): 366 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.95 (3H, t, J=7.3Hz), 1.64-
10 1.70 (2H, m), 2.40-2.43 (2H, m), 5.55 (1H, s), 7.31 (1H, s), 7.54-
7.56 (2H, m), 7.74 (1H, dd, J=3.6, 5.6Hz), 9.93 (1H, s), 12.22 (1H, s).

Example 202

4-(2-Chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from benzoic acid, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>250°C.

Anal. Calcd. for: C₂₀H₁₂ClF₃N₄: C, 59.94; H, 3.02; N, 13.98.

20 Found: C, 59.74; H, 3.18; N, 13.95.

MS (EI): 400 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 5.70 (1H, s), 7.39 (1H, s), 7.49-
7.51 (3H, m), 7.57-7.62 (3H, m), 7.75-7.79 (2H, m), 10.18 (1H, s),
12.31 (1H, s).

25 **Example 203**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as
30 in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₅ClN₄: C, 64.32; H, 5.06; N, 18.75.

Found: C, 64.18; H, 5.12; N, 18.84.

MS (EI) : 298 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.23 (3H, d, J=6.8Hz),
1.27 (3H, d, J=6.8Hz), 3.06 (1H, m), 5.34 (1H, s), 7.22-7.26 (3H, m),
7.30-7.34 (1H, m), 7.42 (1H, d, J=7.1Hz), 9.63 (1H, s), 12.16 (1H, s) .

5 **Example 204**

Ethyl 1-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of the compound (1.2 g) described in Example 27 and dimethylaminopyridine (128 mg) in THF (40 ml)
10 was added di-tert-butyl dicarbonate (830 mg) and the mixture was stirred at room temperature for one day. The solvent was evaporated under reduced pressure and the title compound (102 mg) was obtained as colorless crystals by silica gel column chromatography (eluent: hexane-ethyl acetate (3:1)) .

15 MP: 112-116°C.

Anal. Calcd. for: C₂₃H₂₈ClN₃O₄: C, 61.95; H, 6.33; N, 9.42.

Found: C, 61.84; H, 6.33; N, 9.34.

MS (EI) : 445 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.87 (3H, t, J=6.9Hz),
20 0.98 (3H, t, J=7.3Hz), 1.56 (9H, s), 1.62-1.72 (2H, m), 2.80-
2.92 (2H, m), 3.85 (2H, q, J=6.9Hz), 5.56 (1H, s), 7.14-7.17 (2H, m),
7.23 (1H, dd, J=7.3 and 7.8Hz), 7.30 (1H, s), 7.39 (1H, d, J=7.4Hz),
8.75 (1H, s) .

Example 205

25 Ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 204 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound (300 mg) was obtained
30 as colorless crystals.

MP: 144-147°C.

Anal. Calcd. for: C₂₃H₂₈ClN₃O₄: C, 61.95; H, 6.33; N, 9.42.

Found: C, 61.93; H, 6.35; N, 9.40.

MS (EI) : 445 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 0.85 (3H, t, $J=6.9\text{Hz}$) ,
0.97 (3H, t, $J=7.3\text{Hz}$) , 1.49 (9H, s) , 1.63-1.69 (2H, m) , 2.66-
2.85 (2H, m) , 3.80 (2H, q, $J=6.9\text{Hz}$) , 5.57 (1H, s) , 7.10-7.15 (1H, m) ,
5 7.17 (1H, ddd, $J=1.5$, 7.3 and 7.8Hz) , 7.23 (1H, dd, $J=6.4$ and 7.3Hz) ,
7.41 (1H, d, $J=7.2\text{Hz}$) , 7.67 (1H, s) , 10.01 (1H, s) .

Example 206

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-methoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

10 The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and methyl chloroformate in the same manner as in Example 204.
MS (EI) : 403 (M^+) .

15 IR (KBr) : $\nu=3422, 1736, 1699, 1531, 1450, 1232, 1086\text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 0.87 (3H, t, $J=7.1\text{Hz}$) ,
0.97 (3H, t, $J=7.3\text{Hz}$) , 1.60-1.66 (2H, m) , 2.86-2.89 (2H, m) ,
3.83 (2H, q, $J=7.1\text{Hz}$) , 3.94 (3H, s) , 5.55 (1H, s) , 7.13-7.38 (4H, m) ,
7.35 (1H, s) , 8.67 (1H, s) .

20 Example 207

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-methoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 206 was further flowed hexane-ethyl acetate
25 (3:1) as an eluent, the title compound was obtained as colorless crystals.

MP: 141-143°C.

MS (EI) : 403 (M^+) .

IR (KBr) : $\nu=3290, 1774, 1695, 1633, 1597, 1523, 1444, 1364, 1307, 1209$
30 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 0.86 (3H, t, $J=7.1\text{Hz}$) ,
0.95 (3H, t, $J=7.3\text{Hz}$) , 1.64-1.70 (2H, m) , 2.71-2.85 (2H, m) ,
3.78 (2H, q, $J=7.1\text{Hz}$) , 3.85 (1H, s) , 5.57 (1H, s) , 7.10-7.24 (3H, m) ,

7.42 (1H, d, J=1.4Hz), 7.72 (1H, s), 9.94 (1H, s).

Example 208

Ethyl 1-benzyloxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzyl chloroformate in the same manner as in Example 204. MP: 80°C.

10 Anal. Calcd. for: C₂₆H₂₆ClN₃O₄: C, 65.07; H, 5.46; N, 8.75.

Found: C, 65.24; H, 5.71; N, 8.50.

MS (EI): 479 (M⁺).

IR (KBr): ν =3344, 1745, 1701, 1527, 1451, 1226, 1084, 1060 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88 (3H, t, J=7.0Hz),
15 0.94 (3H, t, J=7.3Hz), 1.56-1.62 (2H, m), 2.81-2.88 (2H, m),
3.82 (2H, q, J=7.0Hz), 5.41 (2H, s), 5.55 (1H, s), 7.13-7.24 (3H, m),
7.36 (1H, s), 7.37 (6H, m), 8.62 (1H, s).

Example 209

Ethyl 2-benzyloxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 Further elution using the column of silica gel column chromatography in Example 208 and hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

25 MS (EI): 479 (M⁺).

IR (KBr): ν =3294, 1759, 1697, 1601, 1383, 1363, 1300, 1201 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.85 (3H, t, J=7.0Hz),
0.95 (3H, t, J=7.3Hz), 1.61-1.67 (2H, m), 2.72-2.82 (2H, m),
3.79 (2H, q, J=7.0Hz), 5.30 (2H, s), 5.56 (1H, s), 7.09-7.41 (9H, m),
30 7.73 (1H, s), 9.95 (1H, s).

Example 210

Ethyl 1-benzoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzoyl chloride in the same manner as in Example 204.

5 MP:115°C.

Anal. Calcd. for: $C_{25}H_{24}ClN_3O_3$: C, 66.74; H, 5.38; N, 9.34.

Found: C, 66.58; H, 5.41; N, 9.28.

MS (EI): 449 (M^+).

IR (KBr): ν =3414, 1680, 1641, 1516, 1095 cm^{-1} .

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90 (3H, t, J =6.3Hz),
1.00 (3H, t, J =7.3Hz), 1.65-1.71 (2H, m), 2.90-2.93 (2H, m),
3.85 (2H, q, J =7.3Hz), 5.63 (1H, s), 7.16-7.22 (2H, m),
7.29 (1H, d, J =7.3Hz), 7.40 (1H, d, J =7.8Hz), 7.46 (1H, s), 7.50-
7.54 (2H, m), 7.65 (1H, dd, J =6.3 and 7.8Hz), 7.98 (1H, d, J =6.3Hz),
15 9.10 (1H, s).

Example 211

Ethyl 2-benzoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography
20 used in Example 210 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MP:119-121°C.

Anal. Calcd. for: $C_{25}H_{24}ClN_3O_3$: C, 66.74; H, 5.38; N, 9.34.

25 Found: C, 66.58; H, 5.43; N, 9.30.

MS (EI): 479 (M^+).

IR (KBr): ν =3406, 1670, 1628, 1601, 1481, 1348, 1084 cm^{-1} .

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, J =6.8Hz),
0.97 (3H, t, J =7.3Hz), 1.65-1.67 (2H, m), 2.74-2.83 (2H, m),
30 3.82 (2H, q, J =7.3Hz), 5.65 (1H, s), 7.13-7.26 (3H, m),
7.44 (1H, d, J =7.8Hz), 7.47-7.51 (2H, m), 7.60 (1H, dd, J =7.3 and
7.3Hz), 7.91 (2H, d, J =7.8), 8.00 (1H, s), 10.06 (1H, s).

Example 212

Ethyl 1-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenylacetyl chloride in the same manner as in Example 204.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89 (3H, t, J=6.8Hz), 0.94 (3H, t, J=7.3Hz), 1.60-1.61 (2H, m), 2.84-2.86 (2H, m), 3.82 (2H, q, J=6.8Hz), 4.47 (2H, s), 5.59 (1H, s), 7.20-9.44 (10H, m),
10 8.90 (1H, s).

Example 213

Ethyl 2-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 212 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS (EI): 463 (M⁺).

IR (KBr): ν=3308, 1699, 1628, 1630, 1599, 1523 cm⁻¹.

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87 (3H, t, J=6.8Hz), 0.98 (3H, t, J=7.3Hz), 1.65-1.71 (2H, m), 2.77-2.84 (2H, m), 3.83 (2H, q, J=6.8Hz), 4.25 (2H, s), 5.60 (1H, s), 7.11-7.31 (8H, m), 7.41 (1H, d, J=7.8Hz), 7.84 (1H, s), 10.30 (1H, s).

Example 214

25 Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-phenylcarbamoyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenyl isocyanate in the same manner as in Example 204.

30 MS (EI): 464 (M⁺).

IR (KBr): ν=3310, 1699, 1597, 1518, 1448, 1369, 1228, 1194, 1093 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.98 (3H, t, J=7.1Hz),

0.97 (3H, t, J=7.3Hz), 1.96 (2H, m), 2.87 (2H, m), 3.83 (2H, q, J=7.1Hz), 5.61 (1H, s), 7.11-7.69 (8H, m), 7.67 (2H, d, J=7.8Hz), 8.86 (1H, s), 10.31 (1H, s).

Example 215

5 Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 214 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as
10 colorless crystals.

MP: 145-147°C.

Anal. Calcd. for: C₂₅H₂₅ClN₄O₃: C, 64.58; H, 5.42; N, 12.05.

Found: C, 64.10; H, 5.41; N, 12.30.

MS (EI): 464 (M⁺).

15 IR (KBr): ν =3341, 1697, 1653, 1630, 1597, 1520, 1367, 1197, 1093 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88 (3H, t, J=7.0Hz), 0.97 (3H, t, J=7.3Hz), 1.68 (2H, m), 2.80-2.92 (2H, m), 3.82 (2H, q, J=7.0Hz), 5.62 (1H, s), 7.10-7.20 (3H, m), 7.22 (1H, dd, J=7.1 and 7.1Hz), 7.31-7.33 (2H, m),
20 7.41 (1H, d, J=7.1Hz), 7.58-7.60 (2H, m), 7.85 (1H, s), 9.67 (1H, s), 9.83 (1H, s).

Example 216

Ethyl 1-benzylcarbamoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzyl isocyanate in the same manner as in Example 204.

MS (EI): 478 (M⁺).

30 IR (KBr): ν =3402, 1699, 1637, 1525, 1226, 1091 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88 (3H, t, J=7.0Hz), 0.96 (3H, t, J=7.3Hz), 1.61-1.63 (2H, m), 2.83 (2H, m), 3.82 (2H, q, J=7.0Hz), 4.37 (2H, d), 5.58 (1H, s), 7.11-7.31 (9H, m),

7.38 (1H, d, J=7.8Hz), 8.74 (1H, s), 9.01 (1H, s).

Example 217

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-phenoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenyl chloroformate in the same manner as in Example 204. MS(EI): 465 (M⁺).

10 IR(KBr): ν =3339, 1728, 1633, 1525, 1371, 1302, 1224, 1091 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.83 (3H, t, J=7.1Hz), 0.96 (3H, t, J=7.3Hz), 1.70 (2H, m), 2.94 (2H, m), 3.82 (2H, q, J=7.1Hz), 5.62 (1H, s), 7.12-7.53 (9H, m), 8.26 (1H, s), 9.30 (1H, s).

Example 218

15 Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-phenoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 217 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as

20 colorless crystals.

MP: 156-157°C.

Anal. Calcd. for: C₂₅H₂₄ClN₃O₄: C, 64.44; H, 5.19; N, 9.02.

Found: C, 64.42; H, 5.31; N, 9.04.

MS(EI): 465 (M⁺).

25 IR(KBr): ν =3325, 1765, 1685, 1597, 1525, 1373, 1205, 1099 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.87 (3H, t, J=7.1Hz), 1.00 (3H, t, J=7.3Hz), 1.67-1.69 (2H, m), 2.76-2.85 (2H, m), 3.82 (2H, q, J=7.1Hz), 5.61 (1H, s), 7.15 (1H, dd, J=1.7 and 6.8Hz), 7.15 (1H, dd, J=1.7 and 6.8Hz), 7.17 (1H, dd, J=2.0 and 7.6Hz),
30 7.24 (1H, dd, J=1.3 and 7.4Hz), 7.27-7.31 (3H, m), 7.41-7.45 (3H, m), 7.89 (1H, s), 10.01 (1H, s).

Example 219

Ethyl 4-(2-chlorophenyl)-1-ethoxycarbonyl-4,7-dihydro-6-

propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and ethyl chloroformate in the same manner as in Example 204.
MP: 88-89°C.

Anal. Calcd. for: C₂₁H₂₄ClN₃O₄: C, 60.36; H, 5.79; N, 10.06.

Found: C, 60.24; H, 5.72; N, 10.05.

MS (EI): 417 (M⁺).

10 IR (KBr): ν = 3422, 1734, 1705, 1647, 1591, 1531, 1228, 1086, 1062 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.87 (3H, t, J=7.1Hz),
0.96 (3H, t, J=7.3Hz), 1.31 (3H, t, J=7.1Hz), 1.61-1.66 (2H, m), 2.83-
2.92 (2H, m), 3.83 (2H, q, J=7.1Hz), 4.41 (2H, q, J=7.1Hz), 5.55 (1H, s),
7.13-7.16 (2H, m), 7.25 (1H, dd, J=7.0 and 7.6Hz), 7.34 (1H, s),
15 7.38 (1H, d, J=7.6Hz), 8.65 (1H, s).

Example 220

Ethyl 4-(2-chlorophenyl)-2-ethoxycarbonyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 219 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS (EI): 417 (M⁺).

IR (KBr): ν = 3325, 1765, 1685, 1631, 1597, 1525, 1373, 1205, 1099 cm⁻¹.

25 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.87 (3H, t, J=7.1Hz),
0.97 (3H, t, J=7.3Hz), 1.26 (3H, t, J=7.0Hz), 1.63-1.69 (2H, m), 2.74-
2.81 (2H, m), 3.81 (2H, q, J=7.1Hz), 4.29 (2H, q, J=7.0Hz), 5.57 (1H, s),
7.12 (1H, dd, J=6.3 and 7.5Hz), 7.17 (1H, d, J=7.8Hz),
7.23 (1H, dd, J=6.3 and 7.4Hz), 7.40 (1H, d, J=7.8Hz), 7.71 (1H, s),
30 9.96 (1H, s).

Example 221

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-propoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and propyl chloroformate in the same manner as in Example 204.

5 MP: 66-68°C.

MS (EI): 431 (M^+).

IR (KBr): ν =3356, 1738, 1695, 1527, 1282, 1084 cm^{-1} .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88 (3H, t, $J=7.0\text{Hz}$),
0.92 (3H, t, $J=7.3\text{Hz}$), 0.97 (3H, t, $J=7.3\text{Hz}$), 1.62-1.67 (2H, m), 1.70-
10 1.75 (2H, m), 2.85-2.92 (2H, m), 3.83 (2H, q, $J=7.0\text{Hz}$),
4.32 (2H, t, $J=6.5\text{Hz}$), 5.57 (1H, s), 7.14-7.18 (2H, m),
7.26 (1H, dd, $J=6.3$ and 7.6Hz), 7.35 (1H, s), 7.39 (1H, d, $J=7.8\text{Hz}$)
9.10 (1H, s).

Example 222

15 Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-propoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 221 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as

20 colorless crystals.

MP: 59°C.

Anal. Calcd. for: $\text{C}_{22}\text{H}_{26}\text{ClN}_3\text{O}_4$: C, 61.18; H, 6.07; N, 9.73.

Found: C, 60.81; H, 5.98; N, 9.74.

MS (EI): 431 (M^+).

25 IR (KBr): ν =3296, 1761, 1697, 1633, 1599, 1523, 1365, 1218, 1089 cm^{-1} .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, $J=7.1\text{Hz}$),
0.89 (3H, t, $J=7.5\text{Hz}$), 0.97 (3H, t, $J=7.3\text{Hz}$), 1.63-1.69 (4H, m), 2.74-
2.81 (2H, m), 3.81 (2H, q, $J=7.1\text{Hz}$), 4.21 (2H, t, $J=6.6\text{Hz}$), 5.58 (1H, s),
7.12 (1H, dd, $J=1.8$ and 7.6Hz), 7.17 (1H, ddd, $J=1.9$, 7.3 and 7.6Hz),
30 7.22 (1H, ddd, $J=1.2$, 7.3 and 7.6Hz), 7.41 (1H, dd, $J=1.2$ and 7.8Hz),
7.72 (1H, s), 9.99 (1H, s).

Example 223

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-isobutyl-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
5 and isobutyryl chloride in the same manner as in Example 204.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84 (3H, t, J=7.0Hz),
0.96 (3H, t, J=7.3Hz), 1.10 (3H, d, J=6.9Hz), 1.14 (3H, d, J=6.8Hz),
1.64-1.70 (2H, m), 2.75-2.83 (2H, m), 3.53 (1H, q, J=7.0Hz),
3.83 (2H, t, J=6.9Hz), 5.59 (1H, s), 7.12 (1H, s), 7.16 (1H, dd, J=5.8
10 and 7.8Hz), 7.24 (1H, dd, J=6.3 and 7.5Hz), 7.41 (1H, s),
7.81 (1H, s), 10.05 (1H, s).

Example 224

Ethyl 1-acetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and acetyl chloride in the same manner as in Example 204.

MP: 75-76°C.

20 Anal. Calcd. for: C₂₀H₂₂ClN₃O₃: C, 61.93; H, 5.72; N, 10.83.

Found: C, 61.77; H, 5.78; N, 10.90.

MS (EI): 387 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89 (3H, t, J=7.3Hz),
0.97 (3H, t, J=7.3Hz), 1.60-1.66 (2H, m), 2.66 (3H, s), 2.85-
25 2.90 (2H, m), 3.81 (2H, q, J=7.3Hz), 5.57 (1H, s), 7.14-7.18 (2H, m),
7.26 (1H, dd, J=7.3 and 7.6Hz), 7.38 (1H, s), 7.39 (1H, d, J=8.1Hz),
8.90 (1H, s).

Example 225

Ethyl 2-acetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 Through the column of silica gel column chromatography used in Example 224 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a

colorless amorphous solid.

MS (EI): 387 (M^+).

IR (KBr): ν =3306, 1699, 1633, 1601, 1523, 1371, 1197, 1086 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.87 (3H, t, $J=7.0\text{Hz}$),

5 0.96 (3H, t, $J=7.3\text{Hz}$), 1.66 (2H, m), 2.44 (3H, s), 2.65-2.85 (2H, m),
3.80 (2H, q, $J=7.0\text{Hz}$), 5.58 (1H, s), 7.09-7.22 (3H, m),
7.40 (1H, d, $J=7.9\text{Hz}$), 7.80 (1H, s), 10.0 (1H, s).

Example 226

Ethyl 1-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-
10 propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and butyl chloroformate in the same manner as in Example 204.

15 MS (EI): 445 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.87 (3H, t, $J=7.3\text{Hz}$),

0.88 (3H, t, $J=7.1\text{Hz}$), 1.33-1.38 (2H, m), 1.60-1.69 (4H, m), 2.85-
2.87 (2H, m), 3.82 (2H, q, $J=7.3\text{Hz}$), 4.36 (2H, t, $J=6.5\text{Hz}$), 5.55 (1H, s),
7.13-7.17 (2H, m), 7.25 (1H, dd, $J=6.4$ and 6.5Hz), 7.34 (1H, s),
20 7.37 (1H, d, $J=7.5\text{Hz}$), 8.61 (1H, s).

Example 227

Ethyl 2-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-
propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography
25 used in Example 226 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS (EI): 445 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.86 (3H, t, $J=7.3\text{Hz}$),

30 0.87 (3H, t, $J=7.3\text{Hz}$), 0.96 (3H, t, $J=7.3\text{Hz}$), 1.31-1.32 (2H, m),
1.61 (4H, m), 2.73-2.80 (2H, m), 3.80 (2H, q, $J=7.3\text{Hz}$),
4.24 (2H, t, $J=6.5\text{Hz}$), 5.57 (1H, s), 7.09-7.22 (3H, m),
7.39 (1H, d, $J=7.8\text{Hz}$), 7.70 (1H, s), 9.98 (1H, s).

Example 228

Ethyl 4-(2-chlorophenyl)-1-cinnamoyl-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and cinnamoyl chloride in the same manner as in Example 204. MP:131-134°C.

Anal. Calcd. for: $C_{27}H_{26}ClN_3O_3$: C, 68.13; H, 5.51; N, 8.83.

10 Found: C, 68.04; H, 5.58; N, 8.75.

MS (EI): 475 (M^+).

IR (KBr): $\nu=3396, 1687, 1624, 1521, 1394, 1207, 1087 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.0\text{Hz}$),
0.98 (3H, t, $J=7.1\text{Hz}$), 1.62-1.68 (2H, m), 2.89-2.91 (2H, m),
15 3.84 (2H, q, $J=7.0\text{Hz}$), 5.60 (1H, s), 7.16 (1H, dd, $J=7.4$ and 7.8Hz),
7.18 (1H, d, $J=6.3\text{Hz}$), 7.26 (1H, dd, $J=6.3$ and 7.4Hz),
7.39 (1H, d, $J=7.8\text{Hz}$), 7.45 (1H, s), 7.46 (3H, m), 7.67 (1H, d, $J=6.1\text{Hz}$),
7.69-7.76 (2H, m), 7.91 (1H, d, $J=7.4\text{Hz}$), 9.01 (1H, s).

Example 229

20 Ethyl 4-(2-chlorophenyl)-1-cinnamoyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 228 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as
25 colorless crystals.

MS (EI): 475 (M^+).

IR (KBr): $\nu=3304, 1695, 1674, 1601, 1521, 1365, 1168, 1095 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.86 (3H, t, $J=7.0\text{Hz}$),
0.98 (3H, t, $J=7.3\text{Hz}$), 1.65-1.70 (2H, m), 2.76-2.87 (2H, m),
30 3.82 (2H, q, $J=7.0\text{Hz}$), 5.62 (1H, s), 7.12-7.18 (2H, m),
7.24 (1H, dd, $J=7.3$ and 7.3Hz), 7.42 (1H, d, $J=7.8\text{Hz}$), 7.45-
7.46 (3H, m), 7.60 (1H, d, $J=6.1\text{Hz}$), 7.62-7.70 (2H, m),
7.86 (1H, d, $J=6.1\text{Hz}$), 7.85 (1H, s), 10.09 (1H, s).

Example 230

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-3-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
5 from 2-ethylbenzaldehyde, 3-amino-5-methylpyrazol and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:164-165°C.

MS (EI):359 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94 (3H, t, J=7.0Hz),
10 1.02 (3H, t, J=7.3Hz), 1.61 (2H, m), 1.89 (3H, s), 2.60-2.85 (2H, m),
3.80 (2H, q, J=7.0Hz), 5.44 (1H, s), 7.00-7.30 (4H, m), 9.39 (1H, s),
11.66 (1H, s).

Example 231

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of ethyl 3-ketohexanoate (7.5 g), 2-chlorobenzaldehyde (6.6 g), piperidine (1.2 g) and acetic acid (2.25 g) in benzene (50 ml) was heated under reflux for 5 hours, and the reaction mixture was dehydrated using a Dean-
20 Stark condenser. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography using an eluent (hexane-ethyl acetate (3:1)) to give ethyl 2-(2-chlorophenyl)methylen-3-oxohexanoate ((E)/(Z)=1:1 mixture) as a yellow oil. A solution of ethyl 2-
25 (2-chlorophenyl)methylene-3-oxohexanoate ((E)/(Z)=1:1 mixture, 2.8 g), 3-amino-1-methylpyrazole (0.25 g) and p-toluenesulfonic acid (25 mg) in toluene (5 mL) and dimethylsulfoxide (0.5 mL) was heated under reflux for one day. The solvent was evaporated under reduced pressure, and the
30 mixture was extracted with ethyl acetate (10 mL) and washed with a saturated aqueous sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give an oil. The

obtained oil was purified by silica gel column chromatography (eluent (ethyl acetate-methanol (10:1))) to give the title compound as colorless crystals.

MP:150-151°C.

5 MS (EI):359 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.83 (3H, t, J=7.0Hz),
0.96 (3H, t, J=6.5Hz), 1.65 (2H, m), 2.67-2.85 (2H, m), 3.58 (3H, s),
3.77 (2H, q, J=7.0Hz), 5.55 (1H, s), 7.07-7.11 (2H, m),
7.19 (1H, dd, J=7.4 and 7.8Hz), 7.24 (1H, d, J=8.3Hz), 9.45 (1H, s).

10 **Example 232**

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-methyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 2-(2-chlorophenyl)methylen-3-oxohexanoate
15 ((E)/(Z)=1:1 mixture), 3-amino-2-methylpyrazole and p-toluenesulfonic acid.

MS (EI):359 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.84 (3H, t, J=7.0Hz),
1.00 (3H, t, J=7.1Hz), 1.67-1.69 (2H, m), 2.70-2.88 (2H, m),
20 3.65 (3H, s), 3.80 (2H, q, J=7.0Hz), 5.55 (1H, s), 6.96 (1H, s), 7.08-
7.12 (2H, m), 7.20 (1H, dd, J=6.8 and 7.8Hz), 7.35 (1H, d, J=7.8Hz),
9.31 (1H, s).

Example 233

Ethyl 4,7-dihydro-1-methyl-4-(naphthalen-1-yl)-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of ethyl 3-ketohexanoate (6.6 g), 1-naphthaldehyde (7.34 g), piperidine (1.2 g) and acetic acid (2.25 g) in benzene (50 mL) was heated under reflux for 3 hours and the reaction mixture was dehydrated using a Dean-
30 Stark condenser. The solvent was evaporated and the residue was purified by silica gel column chromatography using an eluent (hexane-ethyl acetate (3:1)) to give ethyl 2-(naphthalen-1-yl)methylene-3-oxohexanoate ((E)/(Z)=1:1

mixture) as a yellow oil. The title compound was obtained as a colorless amorphous solid from ethyl 2-(naphthalen-1-yl)methylene-3-oxohexanoate ((E)/(Z)=1:1 mixture), 3-amino-2-methylpyrazole and p-toluenesulfonic acid.

5 MS (EI): 375 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.60 (3H, t, $J=6.9\text{Hz}$),
1.03 (3H, t, $J=6.9\text{Hz}$), 1.74 (2H, m), 2.78-2.85 (2H, m), 3.65 (3H, s),
3.68 (2H, q, $J=6.9\text{Hz}$), 5.94 (1H, s), 6.76 (1H, s), 7.20 (1H, d, $J=7.3\text{Hz}$),
7.37 (1H, dd, $J=7.4$ and 7.8Hz), 7.50 (1H, dd, $J=6.9$ and 7.8Hz),
10 7.58 (1H, m), 7.67 (1H, d, $J=8.3\text{Hz}$), 7.88 (1H, d, $J=8.3\text{Hz}$),
8.42 (1H, d, $J=8.8\text{Hz}$), 9.26 (1H, s).

Example 234

Ethyl 4-(3-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was obtained as colorless crystals from 3-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 140-143°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{ClN}_3\text{O}_2 \cdot 2/5 \text{H}_2\text{O}$: C, 61.24; H, 5.94; N, 11.90.

20 Found: C, 61.50; H, 5.94; N, 11.99.

MS (EI): 345 (M^+).

IR (KBr): $\nu=3263, 1736, 1666, 1591, 1514, 1275, 1222, 1207, 1087 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, $J=7.0\text{Hz}$),
1.04 (3H, t, $J=7.1\text{Hz}$), 1.58-1.63 (2H, m), 2.63-2.81 (2H, m),
25 3.86 (2H, q, $J=7.0\text{Hz}$), 5.11 (1H, s), 7.08 (1H, d, $J=7.8\text{Hz}$), 7.12 (2H, m),
7.21 (1H, d, $J=8.3\text{Hz}$), 7.26 (1H, s), 9.84 (1H, s), 11.99 (1H, s).

Example 235

Ethyl 4-(4-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was obtained as colorless crystals from 4-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 159-161°C.

Anal. Calcd. for: $C_{18}H_{20}ClN_3O_2 \cdot 1/5 H_2O$: C, 61.87; H, 5.88; N, 12.03.

Found: C, 61.92; H, 6.23; N, 11.95.

MS (EI) : 345 (M^+).

IR (KBr) : ν =3263, 1730, 1662, 1593, 1516, 1207, 1091 cm^{-1} .

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 0.92 (3H, t, J =7.0Hz),
0.95 (3H, t, J =7.3Hz), 1.60 (2H, m), 2.64-2.80 (2H, m),
3.84 (2H, q, J =7.0Hz), 5.10 (1H, s), 7.13 (2H, d, J =7.3Hz), 7.22 (1H, s),
7.25 (2H, d, J =7.3Hz), 9.45 (1H, s), 11.96 (1H, s).

Example 236

10 Ethyl 4,7-dihydro-4-(4-methyl-1H-imidazol-5-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 4-methyl-5-imidazolecarboxaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

15 MP: 219-220°C.

Anal. Calcd. for: $C_{16}H_{21}N_5O_2 \cdot 1/2 H_2O$: C, 59.61; H, 6.25; N, 21.72.

Found: C, 59.34; H, 6.48; N, 22.06.

MS (EI) : 315 (M^+).

IR (KBr) : ν =3113, 2980, 1687, 1620, 1568, 1244, 1159 cm^{-1} .

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 0.94 (3H, t, J =7.3Hz),
1.08 (3H, t, J =7.0Hz), 1.58-1.59 (2H, m), 2.21 (3H, s), 2.58-
2.79 (2H, m), 3.97 (2H, q, J =7.3Hz), 5.50 (1H, s), 6.14 (1H, s),
7.14 (1H, s), 7.19 (1H, s), 9.78 (1H, s), 11.53 (1H, s).

Example 237

25 Ethyl 4,7-dihydro-4-(1-methyl-1H-imidazol-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 1-methyl-2-imidazolecarboxaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

30 MP: 209°C.

Anal. Calcd. for: $C_{16}H_{21}N_5O_2 \cdot 3/5 H_2O$: C, 59.28; H, 6.28; N, 21.60.

Found: C, 59.00; H, 6.52; N, 21.55.

MS (EI) : 315 (M^+).

IR(KBr): ν =3254, 3184, 3080, 1685, 1593, 1518, 1278, 1207, 1078 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, J =6.8Hz),
0.93 (3H, t, J =7.3Hz), 1.55-1.61 (2H, m), 2.57-2.80 (2H, m),
3.44 (3H, s), 3.87 (2H, q, J =6.8Hz), 5.29 (1H, s), 6.56 (1H, s),
5 6.84 (1H, s), 7.27 (1H, s), 9.38 (1H, s), 11.97 (1H, s).

Example 238

Ethyl 4,7-dihydro-4-(1H-imidazol-5-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
10 from 3-imidazolecarboxyaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 200°C.

Anal. Calcd. for: $\text{C}_{15}\text{H}_{17}\text{N}_5\text{O}_2 \cdot 1/2 \text{H}_2\text{O}$: C, 58.43; H, 5.88; N, 22.71.

Found: C, 58.53; H, 6.25; N, 22.93.

15 MS (EI): 301 (M^+).

IR(KBr): ν =3217, 1655, 1585, 1506, 1226, 1205, 1084 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, J =7.3Hz),
1.01 (3H, t, J =7.3Hz), 1.57-1.59 (2H, m), 2.59-2.74 (2H, m),
3.90 (2H, q, J =7.3Hz), 5.12 (1H, s), 6.35 (1H, s), 7.35 (1H, s),
20 7.38 (1H, s), 9.21 (1H, s), 11.91 (1H, s).

Example 239

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-butyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.
25

MP: 213°C.

Anal. Calcd. for: $\text{C}_{19}\text{H}_{21}\text{N}_5\text{O}_3$: C, 62.11; H, 5.76; N, 19.06.

Found: C, 62.08; H, 5.75; N, 18.95.

30 MS (EI): 367 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.77 (3H, t, J =7.3Hz),
0.92 (3H, t, J =7.3Hz), 1.32-1.40 (2H, m), 1.60-1.64 (2H, m), 2.76-
2.86 (2H, m), 3.76-3.82 (2H, m), 5.68 (1H, s), 7.11 (1H, d, J =6.6Hz),

7.22 (1H, s), 7.51 (1H, dd, J=9.0Hz and 6.6Hz), 7.77 (1H, d, J=9.0Hz), 9.65 (1H, s), 12.00 (1H, s).

Example 240

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate in the same manner as in Example 1.

MP:196°C.

10 Anal. Calcd. for: C₁₇H₁₇N₅O₃: C, 60.17; H, 5.05; N, 20.64.

Found: C, 60.09; H, 5.15; N, 20.41.

MS (EI): 339 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.75 (3H, t, J=7.3Hz), 1.21 (3H, t, J=7.3Hz), 2.83 (2H, q, J=7.3Hz), 3.73-3.84 (2H, m), 5.68 (1H, s),
15 7.12 (1H, d, J=6.6Hz), 7.22 (1H, s), 7.50 (1H, dd, J=9.0Hz and 6.6Hz), 7.77 (1H, d, J=9.0Hz), 9.68 (1H, s), 12.01 (1H, s).

Example 241

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl thiophene-2-carboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:174°C.

Anal. Calcd. for: C₁₇H₁₁ClN₄S 1/10 H₂O: C, 59.94; H, 3.31; N, 16.45.

25 Found: C, 59.82; H, 3.48; N, 16.93.

MS (EI): 338 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 5.50 (1H, s), 7.18 (1H, dd, J=7.3Hz and 7.2Hz), 7.24-7.35 (4H, m), 7.45 (1H, d, J=7.8Hz),
7.60 (1H, d, J=3.6Hz), 7.77 (1H, d, J=3.9Hz), 10.08 (1H, s),
30 12.29 (1H, s).

Example 242

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:215°C.

5 Anal. Calcd. for: $C_{18}H_{14}N_4OS$: C, 64.65; H, 4.22; N, 16.75.

Found: C, 64.66; H, 4.32; N, 17.02.

MS (EI): 334 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.85 (3H, s), 5.34 (1H, s),
6.93 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.01 (1H, d, $J=7.3$ Hz), 7.14-
10 7.25 (4H, m), 7.60 (1H, d, $J=3.6$ Hz), 7.77 (1H, d, $J=5.1$ Hz), 9.91 (1H, s),
12.17 (1H, s).

Example 243

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl thiophene-2-carboxylate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:222°C.

Anal. Calcd. for: $C_{18}H_{14}N_4S_2 \cdot 2/5 H_2O$: C, 60.44; H, 4.17; N, 15.66.

20 Found: C, 60.58; H, 4.44; N, 15.35.

MS (EI): 350 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.49 (3H, s), 5.48 (1H, s), 7.17-
7.28 (5H, m), 7.33 (1H, d, $J=7.3$ Hz), 7.60 (1H, d, $J=3.7$ Hz),
7.77 (1H, d, $J=3.9$ Hz), 10.01 (1H, s), 12.22 (1H, s).

25 Example 244

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-nitrobenzaldehyde and 3-aminopyrazole in the
30 same manner as in Example 95.

MP:165°C.

Anal. Calcd. for: $C_{17}H_{11}N_5O_2S$: C, 58.44; H, 3.17; N, 20.05.

Found: C, 58.15; H, 3.42; N, 20.38.

MS (EI) : 349 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 5.54 (1H, s), 7.18 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.34 (1H, s), 7.48-7.55 (2H, m),
7.60 (1H, d, $J=3.7\text{Hz}$), 7.72-7.79 (2H, m), 7.92 (1H, d, $J=8.1\text{Hz}$),
5 10.16 (1H, s), 12.35 (1H, s) .

Example 245

4-(2,1,3-Benzothiadiazo-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-
10 carboxylate, 2,1,3-benzothiadiazo-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 254°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{10}\text{N}_6\text{S}_2$: C, 56.34; H, 2.78; N, 23.19.

Found: C, 56.01; H, 2.91; N, 23.19.

15 MS (EI) : 362 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 5.84 (1H, s), 7.19 (1H, dd, $J=4.4\text{Hz}$ and 4.3Hz), 7.28 (1H, s), 7.55 (1H, d, $J=6.8\text{Hz}$), 7.65 (1H, d, $J=3.7\text{Hz}$),
7.72-7.79 (2H, m), 7.99 (1H, d, $J=8.8\text{Hz}$), 10.14 (1H, s), 12.21 (1H, s) .

Example 246

20 5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, naphthalene-1-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

25 MP: 214°C.

Anal. Calcd. for: $\text{C}_{21}\text{H}_{14}\text{N}_4\text{S}$: C, 71.16; H, 3.98; N, 15.81.

Found: C, 70.75; H, 3.96; N, 15.85.

MS (EI) : 354 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 5.87 (1H, s), 7.13 (1H, s),
30 7.18 (1H, dd, $J=4.6\text{Hz}$ and 3.9Hz), 7.45-7.54 (4H, m),
7.62 (1H, d, $J=3.9\text{Hz}$), 7.78 (1H, d, $J=4.9\text{Hz}$), 7.83 (1H, d, $J=8.1\text{Hz}$),
7.95 (1H, d, $J=9.3\text{Hz}$), 8.31 (1H, d, $J=7.3\text{Hz}$), 10.09 (1H, s),
12.17 (1H, s) .

Example 247

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:232°C.

Anal. Calcd. for: $C_{17}H_{10}Cl_2N_4S \cdot 1/10 H_2O$: C, 54.44; H, 2.74; N, 14.94.

Found: C, 54.08; H, 2.90; N, 15.29.

10 MS (EI) : 373 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.58 (1H, s), 7.18 (1H, dd, $J=7.3$ Hz and 7.2 Hz), 7.32-7.41 (3H, m), 7.54 (1H, dd, $J=7.3$ Hz and 1.5 Hz), 7.60 (1H, d, $J=3.7$ Hz), 7.78 (1H, d, $J=4.9$ Hz), 10.14 (1H, s), 12.32 (1H, s).

15 **Example 248**

5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:246°C.

Anal. Calcd. for: $C_{20}H_{16}N_4 \cdot 1.0 H_2O$: C, 72.71; H, 5.49; N, 16.96.

Found: C, 72.50; H, 5.26; N, 17.20.

MS (EI) : 312 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.38 (3H, s), 5.29 (1H, s), 7.11-7.23 (5H, m), 7.47-7.49 (3H, m), 7.55-7.58 (2H, m), 9.94 (1H, s), 12.17 (1H, s).

Example 249

30 5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:276°C.

Anal. Calcd. for: C₁₈H₁₄N₄S: C, 67.90; H, 4.43; N, 17.60.

Found: C, 67.93; H, 4.54; N, 17.64.

MS (EI): 318 (M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.36(3H, s), 5.28(1H, s), 7.11-7.18(5H, m), 7.24(1H, s), 7.55(1H, dd, J=3.7Hz and 1.0Hz), 7.74(1H, dd, J=5.9Hz and 1.0Hz), 9.95(1H, s), 12.22(1H, s).

Example 250

4-(2-Chlorophenyl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl dimethoxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.39(6H, s), 5.18(1H, s), 5.43(1H, s), 7.23-7.27(3H, m), 7.32-7.35(1H, m), 7.44(1H, d, J=7.8Hz), 9.65(1H, s), 12.21(1H, s).

Example 251

4-(2-Chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

20 4-(2-Chlorophenyl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (4.4 g) was added to trifluoroacetic acid (20 ml) under ice-cooling and the mixture was stirred at room temperature for 2.5 hours. The reaction mixture was concentrated under reduced pressure and
25 crystallized from ethyl acetate (50 ml) to give the title compound (1.9 g) as yellow crystals.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.63(1H, s), 7.27-7.46(5H, m), 7.48(1H, d, J=7.1Hz), 9.73(1H, s), 10.17(1H, s), 12.34(1H, s).

Example 252

30 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine

To a suspension of 4-(2-chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (400 mg) in methanol

(10 ml) was added sodium borohydride (53 mg) under ice-cooling and the mixture was stirred at the same temperature for 30 minutes. 10% Hydrochloric acid was added to the reaction mixture, and a saturated sodium hydrogencarbonate solution was
5 added. The precipitated crystals were collected by filtration and washed with ethanol to give the title compound (295 mg) as yellow crystals.

MP:205-210°C (decomposition).

Anal. Calcd. for: $C_{14}H_{11}ClN_4O \cdot \frac{1}{4} H_2O$: C, 57.74; H, 3.98; N, 19.24.

10 Found: C, 57.38; H, 3.93; N, 18.94.

MS(EI): 286 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 4.29 (2H, d, $J=5.6$ Hz), 5.38 (1H, s), 5.49 (1H, t, $J=5.6$ Hz), 7.22-7.34 (4H, m), 7.43 (1H, d, $J=8.0$ Hz), 9.60 (1H, s), 12.17 (1H, s).

15 **Example 253**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonyl-ethenyl)-2H-pyrazolo[3,4-b]pyridine

To a suspension of sodium hydride (94 mg) in dimethoxyethane (10 ml) was added ethyl
20 diethylphosphonoacetate (528 mg) and the mixture was stirred at room temperature for 15 minutes. Under ice-cooling, 4-(2-chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (670 mg) was added to the mixture, and the mixture was stirred at the same temperature for 1 hour. Water was
25 added to the reaction mixture and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography
30 (eluent: hexane-ethyl acetate (1:1)) to give the title compound (560 mg) as yellow crystals.

MP:240-243°C (decomposition).

Anal. Calcd. for: $C_{18}H_{15}ClN_4O_2 \cdot \frac{1}{2} H_2O$: C, 59.43; H, 4.43; N, 15.40.

Found: C, 59.53; H, 4.26; N, 15.31.

MS (EI) : 354 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.25 (3H, d, J=7.1Hz),
4.21 (2H, q, J=7.1Hz), 5.52 (1H, s), 6.93 (1H, d, J=15.9Hz), 7.27-
5 7.46 (6H, m), 10.09 (1H, s), 12.31 (1H, s).

Example 254

4-(2-Chlorophenyl)-5-cyano-6-(2-ethoxycarbonylethyl)-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine

A suspension of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-
10 6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine
(260 mg) and 5% palladium on carbon (110 mg) in ethanol was
subjected to catalytic hydrogenation at room temperature for 5
hours. The reaction mixture was filtered through Celite and
the filtrate was concentrated under reduced pressure. The
15 obtained residue was purified by silica gel column
chromatography (eluent: hexane-ethyl acetate (1:1)) to give a
yellow solid. The yellow solid was crystallized from ethyl
acetate-diisopropyl ether to give the title compound (160 mg)
as pale-yellow crystals.

20 MP: 172-174°C.

MS (EI) : 356 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.18 (3H, t, J=7.3Hz), 2.60-
2.80 (4H, m), 4.08 (2H, q, J=7.3Hz), 5.35 (1H, s), 7.20-7.31 (4H, m),
7.42 (1H, d, J=8.0Hz), 9.84 (1H, s), 12.16 (1H, s).

25 Example 255

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-dimethoxymethyl-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
dimethoxyacetate, 2,1,3-benzoxadiazole-4-aldehyde and 3-
30 aminopyrazole in the same manner as in Example 94.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 3.35 (3H, s), 3.38 (3H, s),
5.16 (1H, s), 5.47 (1H, s), 7.26 (1H, s), 7.42 (1H, d, J=6.6Hz),
7.60 (1H, dd, J=6.6, 8.5Hz), 7.94 (1H, d, J=8.5Hz), 9.77 (1H, s),

12.19(1H,s).

Example 256

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 251.
¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.71(1H,s), 7.33(1H,s),
7.56(1H,d, J=6.6Hz), 7.62(1H,dd, J=6.6, 8.8Hz),
10 7.98(1H,d, J=8.8Hz), 9.73(1H,s), 10.32(1H,s), 12.32(1H,s).

Example 257

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 252.
MP:215-220°C (decomposition).
Anal. Calcd. for: C₁₄H₁₀N₆O₂ 1/2 H₂O: C, 55.44; H, 3.66; N, 27.71.
Found: C, 55.32; H, 3.68; N, 27.31.

20 MS (EI): 294 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 4.30(2H,s), 5.45(1H,s),
5.52(1H,brs), 7.27(1H,s), 7.42(1H,d, J=6.6Hz),
7.59(1H,dd, J=6.6, 9.0Hz), 7.93(1H,d, J=9.0Hz), 9.71(1H,s),
12.16(1H,s).

25 **Example 258**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonyl-ethenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 253.
30 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.24(3H,d, J=7.1Hz),
4.21(2H,q, J=7.1Hz), 5.59(1H,s), 6.96(1H,d, J=16.1Hz),
7.32(1H,s), 7.39(1H,d, J=16.1Hz), 7.50(1H,m), 7.59(1H,m),

7.96(1H,d,J=8.3Hz), 10.21(1H,s), 12.29(1H,s).

Example 259

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(2-ethoxycarbonylethyl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 254.

MS(EI):364(M⁺).

10 ¹H-NMR (400MHz,DMSO-d₆) δ(ppm): 1.18(3H,t,J=7.1Hz), 2.66-2.80(4H,m), 4.08(2H,q,J=7.1Hz), 5.40(1H,s), 7.26(1H,s), 7.42(1H,d,J=6.6Hz), 7.58(1H,dd,J=6.6,9.0Hz), 7.92(1H,d,J=9.0Hz), 9.96(1H,s), 12.16(1H,s).

Example 260

15 4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

 The title compound was prepared from methyl isobutyrate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

20 MP:>250°C.

Anal. Calcd. for:C₁₇H₁₄BrN₅:C,55.45;H,3.83;N,19.02.

Found:C,55.30;H,3.91;N,18.98.

MS(EI):368(M⁺).

25 ¹H-NMR (400MHz,DMSO-d₆) δ(ppm): 1.23(3H,d,J=6.8Hz), 1.27(3H,d,J=6.8Hz), 3.03(1H,m), 5.45(1H,s), 7.33(1H,s), 7.55-7.82(2H,m), 7.83(1H,dd,J=2.0,7.1Hz), 9.76(1H,s), 12.25(1H,s).

Example 261

4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine acetonitrile

30 The title compound was prepared from methyl isobutyrate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: $C_{16}H_{15}BrN_4C_2H_3N$: C, 56.26; H, 4.72; N, 18.22.

Found: C, 56.05; H, 4.56; N, 17.09.

MS(EI): 343 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.24 (3H, d, $J=7.1$ Hz),
5 1.27 (3H, d, $J=7.1$ Hz), 2.06 (3H, s), 3.06 (1H, m), 5.23 (1H, s), 7.13-
7.18 (1H, m), 7.22 (1H, d, $J=7.6$ Hz), 7.27 (1H, s),
7.36 (1H, dd, $J=1.2, 7.6$ Hz), 7.59 (1H, dd, $J=1.2, 8.0$ Hz), 9.64 (1H, s),
12.17 (1H, s).

Example 262

10 5-Cyano-4,7-dihydro-6-isopropyl-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 MP: 224°C.

MS(EI): 309 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.23 (3H, d, $J=7.1$ Hz),
1.28 (3H, d, $J=7.1$ Hz), 3.03 (1H, m), 5.36 (1H, s), 7.27 (1H, s), 7.43-
7.49 (2H, m), 7.70 (1H, dd, $J=1.2, 8.8$ Hz), 7.89 (1H, dd, $J=1.2, 8.3$ Hz),
20 9.71 (1H, s), 12.23 (1H, s).

Example 263

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
25 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: >250°C.

Anal. Calcd. for: $C_{16}H_{14}Cl_2N_4$: C, 57.67; H, 4.23; N, 16.89.

Found: C, 57.74; H, 4.27; N, 16.89.

30 MS(EI): 333 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.23 (3H, d, $J=7.1$ Hz),
1.27 (3H, d, $J=7.1$ Hz), 3.04 (1H, m), 5.42 (1H, s), 7.23 (1H, d, $J=7.6$ Hz),
7.31 (1H, s), 7.35 (1H, dd, $J=7.6, 7.8$ Hz), 7.51 (1H, dd, $J=1.5, 7.8$ Hz),

9.70(1H,s), 12.21(1H,s).

Example 264

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl isobutyrate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:222-223°C (decomposition).

Anal. Calcd. for: C₁₆H₁₄N₆O: C, 62.71; H, 4.61; N, 27.44.

10 Found: C, 62.71; H, 4.65; N, 27.45.

MS (EI): 306 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.24 (3H, d, J=7.1Hz),
1.25 (3H, d, J=7.1Hz), 3.03 (1H, m), 5.39 (1H, s), 7.26 (1H, s),
7.40 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=6.6, 8.8Hz),
15 7.92 (1H, d, J=8.8Hz), 9.74 (1H, s), 12.15 (1H, s).

Example 265

5-Cyano-4,7-dihydro-6-isopropyl-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
20 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₈N₄O: C, 69.37; H, 6.16; N, 19.03.

Found: C, 69.13; H, 6.21; N, 19.54.

25 MS (EI): 294 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23 (3H, d, J=7.1Hz),
1.28 (3H, d, J=7.1Hz), 3.09 (1H, m), 3.83 (3H, s), 5.19 (1H, s),
6.90 (1H, dd, J=7.4, 7.6Hz), 6.99 (1H, d, J=7.6Hz),
7.05 (1H, dd, J=1.7, 7.4Hz), 7.15-7.19 (2H, m), 9.47 (1H, s),
30 12.04 (1H, s).

Example 266

4-(2-Chlorophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

5 Anal. Calcd. for: $C_{16}H_{13}ClN_4$: C, 64.76; H, 4.42; N, 18.88.

Found: C, 64.71; H, 4.50; N, 19.05.

MS(EI): 296 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89-0.93 (2H, m), 1.00-1.15 (2H, m),
2.01 (1H, m), 5.35 (1H, s), 7.22-7.26 (3H, m), 7.31-7.34 (1H, m),
10 7.42 (1H, d, J=7.8Hz), 9.14 (1H, s), 12.16 (1H, s).

Example 267

4-(2-Bromophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
15 cyclopropanecarboxylate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: $C_{16}H_{13}BrN_4$: C, 56.32; H, 3.84; N, 16.42.

Found: C, 56.18; H, 3.90; N, 16.48.

20 MS(EI): 341 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.93 (2H, m), 1.00-1.15 (2H, m),
2.01 (1H, m), 5.34 (1H, s), 7.13-7.22 (2H, m), 7.27 (1H, s), 7.34-
7.38 (1H, m), 7.59 (1H, d, J=6.8Hz), 9.15 (1H, s), 12.16 (1H, s).

Example 268

25 4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

30 MP:>250°C.

Anal. Calcd. for: $C_{17}H_{12}BrN_5H_2O$ 1/4 CH_3CN : C, 53.28; H, 3.77; N, 18.64.

Found.: C, 53.28; H, 3.72; N, 18.81.

MS(EI): 366 (M^+).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.90-0.93 (2H, m), 1.03-1.08 (2H, m), 1.96-2.00 (1H, m), 5.45 (1H, s), 7.32 (1H, s), 7.54-7.60 (2H, m), 7.83 (1H, dd, J=1.7, 7.1Hz), 9.27 (1H, s), 12.25 (1H, s).

Example 269

5 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

10 MP: 200-201°C (decomposition).

Anal. Calcd. for: C₁₆H₁₂N₆O · H₂O: C, 59.62; H, 4.38; N, 26.07.

Found: C, 59.93; H, 4.05; N, 26.19.

MS (EI): 304 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88-0.93 (2H, m), 1.01-1.12 (2H, m),
15 1.99 (1H, m), 5.39 (1H, s), 7.25 (1H, s), 7.40 (1H, d, J=6.6Hz),
7.59 (1H, dd, J=6.6, 9.0Hz), 7.92 (1H, d, J=9.0Hz), 9.26 (1H, s),
12.15 (1H, s).

Example 270

20 4-(2-Methoxyphenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 241-243°C.

25 Anal. Calcd. for: C₁₇H₁₆N₄O 1/4 CH₃CN: C, 69.46; H, 5.58; N, 19.67.

Found: C, 69.35; H, 5.56; N, 19.64.

MS (EI): 292 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.90-0.92 (2H, m), 0.99-1.10 (2H, m),
2.01-2.06 (1H, m), 3.84 (3H, s), 5.21 (1H, s),
30 6.90 (1H, dd, J=7.3, 7.6Hz), 6.98-7.05 (2H, m), 7.15-7.19 (2H, m),
8.97 (1H, s), 12.04 (1H, s).

Example 271

5-Cyano-6-cyclopropyl-4-(2,3-dichlorophenyl)-4,7-dihydro-2H-

pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP: >250°C.

Anal. Calcd. for: $C_{16}H_{12}Cl_2N_4 \cdot 1/4 CH_3CN$: C, 58.04; H, 3.76; N, 17.43.

Found: C, 57.87; H, 3.79; N, 17.44.

MS (EI): 331 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.93 (2H, m), 1.03-1.08 (2H, m),
10 1.98-2.03 (1H, m), 5.43 (1H, s), 7.22 (1H, d, J=7.8Hz), 7.31 (1H, s),
7.35 (1H, t, J=7.8Hz), 7.51 (1H, dd, J=1.5, 7.8Hz), 9.21 (1H, s),
12.20 (1H, s).

Example 272

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(2-nitrophenyl)-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 236-238°C (decomposition).

20 Anal. Calcd. for: $C_{16}H_{13}N_5O_2$: C, 62.53; H, 4.26; N, 22.79.

Found: C, 62.54; H, 4.29; N, 22.85.

MS (EI): 307 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.93 (2H, m), 1.01-1.09 (2H, m),
1.99 (1H, m), 5.37 (1H, s), 7.27 (1H, s), 7.42-7.49 (2H, m),
25 7.70 (1H, dd, J=7.5, 7.6Hz), 7.90 (1H, d, J=8.1Hz), 9.23 (1H, s),
12.22 (1H, s).

Example 273

Ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4,4-dimethoxy-3-oxobutanoate in the same manner as in Example 1.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87 (3H, t, J=7.1Hz), 3.35 (3H, s),

3.46(3H,s), 3.82(2H,m), 5.64(1H,s), 6.11(1H,s), 7.10-7.14(2H,m),
7.20-7.24(1H,m), 7.27(1H,s), 7.36(1H,d,J=8.3Hz), 8.94(1H,s),
12.05(1H,s).

Example 274

5 Ethyl 4-(2-chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (463 mg) in tetrahydrofuran (5 ml) was added 1N
10 hydrochloric acid (10 ml) and the mixture was stirred at room temperature for 6 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and
15 dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (290 mg) as a yellow solid.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H,t,J=7.3Hz), 3.91(2H,m),
20 5.70(1H,s), 7.14-7.24(3H,m), 7.31(1H,s), 7.40(1H,d,J=7.8Hz), 9.64(1H,s), 10.23(1H,s), 12.19(1H,s).

Example 275

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 2-Chlorobenzaldehyde (1.41 g), 3-aminopyrazole (0.83 g) and ethyl isobutyrylacetate (1.58 g) were stirred in acetic acid (10 ml) at 80°C for 2 hours. Under ice-cooling, a saturated aqueous sodium hydrogencarbonate solution was added to the reaction mixture. The insoluble material was filtered
30 off, and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the

obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)). The purified product was crystallized from hexane-ethyl acetate to give the title compound (115 mg) as white crystals.

5 MP:211-213°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.1Hz), 1.16(3H, m), 1.28(3H, d, J=7.1Hz), 3.76(2H, m), 4.35(1H, m), 5.59(1H, s), 7.07-7.13(2H, m), 7.18-7.22(1H, m), 7.24(1H, s), 7.35(1H, dd, J=1.2, 8.1Hz), 9.14(1H, s), 11.97(1H, s).

10 **Example 276**

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromobenzaldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner
15 as in Example 275.

MP:214-215°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=6.8Hz), 1.16(3H, m), 1.28(3H, d, J=6.8Hz), 3.76(2H, m), 4.35(1H, m), 5.56(1H, s), 7.07-7.13(2H, m), 7.02(1H, dd, J=7.3, 7.8Hz), 7.11(1H, d, J=6.4Hz),
20 7.24(1H, dd, J=7.4, 7.8Hz), 7.28(1H, s), 7.52(1H, d, J=7.8Hz), 9.15(1H, s), 11.98(1H, s).

Example 277

Ethyl 4-(2-chlorophenyl)-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 To a solution of 2-oxazolydone (20.8 g) in tetrahydrofuran (750 ml) was added n-butyllithium (1.56 M hexane solution, 153 ml) at -78°C and the mixture was stirred at the same temperature for 30 minutes. To the reaction mixture was added a solution of cyclopropanecarbonyl chloride
30 (25 g) in tetrahydrofuran (50 ml) at -78°C over 30 minutes. The mixture was stirred for 14 hours while gradually raising the temperature to room temperature. The reaction mixture was poured into ice-water and the mixture was extracted with ethyl

acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give white crystals (26 g). A mixture of the obtained white crystals (10 g), ethyl bromoacetate (21.5 ml) and zinc powder (25.3 g) in tetrahydrofuran (300 ml) was ultrasonicated for 2 hours and heated under reflux for 2 hours. To the reaction mixture was added 10% hydrochloric acid and the insoluble material was filtered off through Celite. The filtrate was extracted with ethyl acetate, and the extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give ethyl 3-cyclopropyl-3-oxopropionate (5.7 g) as a yellow oil. Subsequently, the title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-cyclopropyl-3-oxopropionate in the same manner as in Example 275.

MP:190-192°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83-0.93(4H, m), 1.10(1H, m), 3.14(1H, m), 3.80(2H, m), 5.60(1H, s), 7.08-7.12(2H, m), 7.18-7.22(1H, m), 7.25(1H, s), 7.34(1H, d, J=8.3Hz), 8.62(1H, s), 11.99(1H, s).

Example 278

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>280°C.

Anal. Calcd. for: $C_{18}H_{10}BrN_5S$: C, 52.95; H, 2.47; N, 17.15.

Found: C, 52.72; H, 2.69; N, 17.21.

MS (EI): 408 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.62 (1H, s), 7.18 (1H, dd, $J=5.1$ Hz and 3.7 Hz), 7.40 (1H, s), 7.59-7.67 (3H, m), 7.79 (1H, d, $J=3.9$ Hz), 7.86 (1H, dd, $J=7.6$ Hz and 2.0 Hz), 10.20 (1H, s), 12.37 (1H, s).

Example 279

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl butanoate 2-chlorobenzaldehyde and 3-amino-5-methylpyrazole in the same manner as in Example 94.

MP: 260°C.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, $J=7.3$ Hz), 1.60-
15 1.65 (2H, m), 1.71 (3H, s), 2.33 (2H, q, $J=7.3$ Hz), 5.27 (1H, s), 7.20-7.24 (2H, m), 7.31 (1H, dd, $J=7.3$ Hz and 7.2 Hz), 7.39 (1H, d, $J=7.3$ Hz), 9.68 (1H, s), 11.83 (1H, s).

Example 280

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl butanoate 2-chlorobenzaldehyde and 3-amino-5-phenylpyrazole in the same manner as in Example 94.

MP: 262°C.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.3$ Hz), 1.61-
25 1.63 (2H, m), 2.36 (2H, q, $J=7.3$ Hz), 5.61 (1H, s), 7.09-7.34 (9H, m), 9.89 (1H, s), 12.62 (1H, s).

Example 281

1-tert-Butoxycarbonyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine

30 The title compound was obtained as a colorless amorphous solid from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and di-tert-

butyl dicarbonate in the same manner as in Example 204.

MP:98-102°C.

MS (EI) :398 (M⁺) .

IR (KBr) : ν =3391, 2199, 1723, 1643, 1529, 1394, 1149 cm⁻¹.

5 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.95 (3H, t, J=7.3Hz), 1.57 (3H, s),
1.60-1.67 (2H, m), 2.53-2.61 (2H, m), 5.38 (1H, s), 7.25-7.31 (3H, m),
7.35 (1H, ddd, J=1.4, 7.3 and 7.8Hz), 7.45 (1H, d, J=8.1Hz),
9.20 (1H, s) .

Example 282

10 2-tert-Butoxycarbonyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

Through the column of silica gel column chromatography used in Example 281 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as

15 colorless crystals.

MP:175°C (decomposition).

Anal. Calcd. for: C₂₁H₂₃ClN₄O₂: C, 63.23; H, 5.81; N, 14.05.

Found: C, 62.91; H, 5.80; N, 13.82.

MS (EI) :398 (M⁺) .

20 IR (KBr) : ν =3329, 2197, 1747, 1612, 1523, 1369, 1311, 1151, 949 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.93 (3H, t, J=7.4Hz),
1.65 (2H, q, J=7.3Hz), 2.40-2.44 (2H, m), 2.48 (9H, s), 5.32 (1H, s),
7.27-7.36 (3H, m), 7.45 (1H, d, J=7.8Hz), 7.68 (1H, s), 10.32 (1H, s) .

Example 283

25 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-1-phenylcarbamoyl-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as a colorless amorphous solid from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenyl

30 isocyanate in the same manner as in Example 204.

MP:138-140°C.

Anal. Calcd. for: C₂₃H₂₀ClN₅O 1/4 H₂O: C, 65.4; H, 4.89; N, 16.58.

Found: C, 65.20; H, 5.05; N, 16.17

MS (EI) : 417 (M^+) .

IR (KBr) : ν =3387, 3294, 2202, 1712, 1537 cm^{-1} .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 0.95 (3H, t, J =7.3Hz) ,

1.63 (2H, q, J =7.4Hz) , 2.58 (2H, m) , 5.43 (1H, s) , 7.13 (1H, dd, J =7.4

5 and 7.5Hz) , 7.24-7.36 (6H, m) , 7.46 (1H, d, J =7.8Hz) ,

7.69 (2H, d, J =7.8Hz) , 9.46 (1H, s) , 10.38 (1H, s) .

Example 284

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

10 Through the column of silica gel column chromatography used in Example 283 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless oil.

MP: 167-171°C.

15 MS (EI) : 417 (M^+) .

IR (KBr) : ν =3215, 2204, 1732, 1631, 1523, 1375 cm^{-1} .

^1H -NMR (400MHz, DMSO- d_6) δ (ppm) : 0.97 (3H, t, J =7.4Hz) ,

1.65 (2H, q, J =7.3Hz) , 2.48 (2H, m) , 5.39 (1H, s) , 6.95 (1H, dd, J =7.3

and 7.3Hz) , 7.11 (2H, dd, J =7.3 and 7.6Hz) , 7.24-7.49 (4H, m) ,

20 7.61 (2H, d, J =7.8Hz) , 7.88 (1H, s) , 8.63 (1H, s) , 9.77 (1H, s) ,

10.17 (1H, s) .

Example 285

2-Acetoxyacetyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

25 The title compound was obtained as colorless crystals from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and acetoxyacetyl chloride in the same manner as in Example 204.

MP: 149-150°C.

30 Anal. Calcd. for: $\text{C}_{20}\text{H}_{19}\text{ClN}_4\text{O}_3$: C, 60.23; H, 4.80; N, 14.05.

Found: C, 60.17; H, 4.83; N, 13.90.

MS (EI) : 398 (M^+) .

IR (KBr) : ν =3281, 3238, 2197, 1745, 1630, 1608, 1523, 1385, 1344, 1236,

1172 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.95 (3H, t, $J=7.3\text{Hz}$), 1.64-
1.70 (2H, m), 2.44 (2H, q, $J=7.3\text{Hz}$), 3.33 (3H, s), 5.26 (2H, s),
5.37 (1H, s), 7.29-7.35 (3H, m), 7.46 (1H, d, $J=7.8\text{Hz}$), 7.86 (1H, s),
5 10.45 (1H, s).

Example 286

Ethyl 1-acetoxyacetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl- 1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
10 from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
and acetoxyacetyl chloride in the same manner as in Example
204.

MP: 130-131°C.

15 Anal. Calcd. for: $\text{C}_{22}\text{H}_{24}\text{ClN}_3\text{O}_5$: C, 59.26; H, 5.43; N, 9.42.

Found: C, 59.17; H, 5.39; N, 9.31.

MS (EI): 445 (M^+).

IR (KBr): $\nu=3337, 1732, 1529, 1390, 1246, 1086 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.88 (3H, t, $J=7.0\text{Hz}$),
20 0.97 (3H, t, $J=7.3\text{Hz}$), 1.64-1.70 (2H, m), 2.76-2.82 (2H, m),
3.31 (3H, s), 3.85 (2H, q, $J=7.0\text{Hz}$), 5.27 (2H, dd, $J=3.0$ and 9.8Hz),
5.60 (1H, s), 7.10-7.25 (3H, m), 7.41 (1H, dd, $J=1.4$ and 8.0Hz),
7.82 (1H, s), 10.1 (1H, s).

Example 287

Ethyl 1-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6- propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
30 and phenylacetyl chloride in the same manner as in Example 204.

MS (EI): 463 (M^+).

IR (KBr): $\nu=3418, 1701, 1521, 1392, 1228 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.88 (3H, t, $J=7.0\text{Hz}$),

0.93 (3H, t, J=7.3Hz), 1.57-1.62 (2H, m), 2.80-2.87 (2H, m),
3.82 (2H, q, J=7.0Hz), 4.33 (2H, s), 5.57 (1H, s), 7.15 (1H, dd, J=7.4
and 7.8Hz), 7.18-7.31 (7H, m), 7.39 (1H, d, J=7.8Hz), 7.44 (1H, s),
8.94 (1H, s).

5 **Example 288**

4-(2,1,3-Benzoxadiazol-4-yl)-2-tert-butoxycarbonyl-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-
10 propyl-1H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and
tert-butyldicarbonate in the same manner as in Example 204.
MP: 168-170°C.

Anal. Calcd. for: C₂₁H₂₂N₆O₃: C, 62.06; H, 5.46; N, 20.68.

Found: C, 61.92; H, 5.44; N, 20.52.

15 MS (EI): 406 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.89 (3H, t, J=7.3Hz), 1.47 (9H, s),
1.65 (2H, m), 2.40 (2H, m), 5.39 (1H, s), 7.49 (1H, d, J=6.3Hz),
7.60 (1H, dd, J=6.6 and 9.0Hz), 7.79 (1H, s), 7.96 (1H, d, J=6.6Hz),
10.43 (1H, s).

20 **Example 289**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-1-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-
25 propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and
phenyl isocyanate in the same manner as in Example 204.

MP: 138-140°C.

Anal. Calcd. for: C₂₃H₁₉N₇O₂: C, 64.93; H, 4.50; N, 23.05.

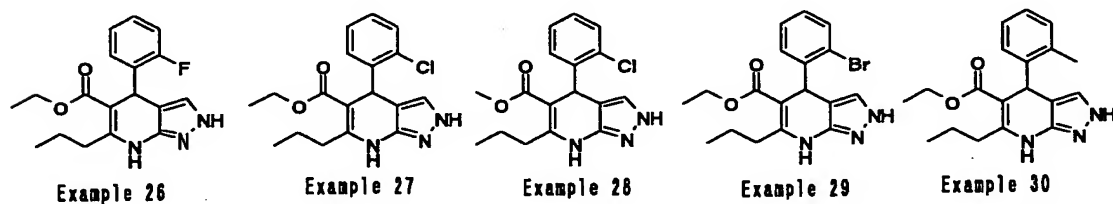
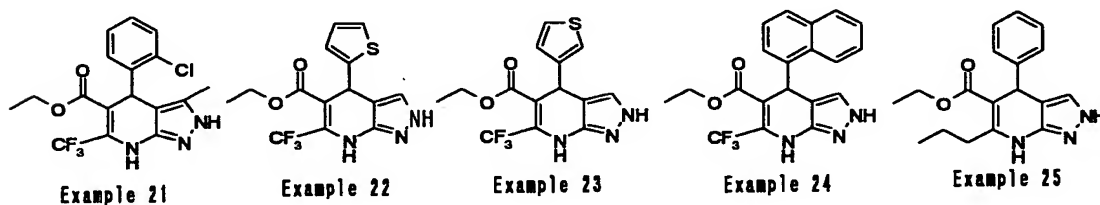
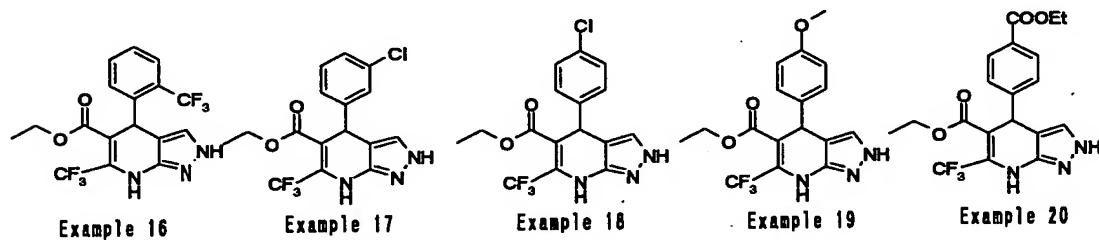
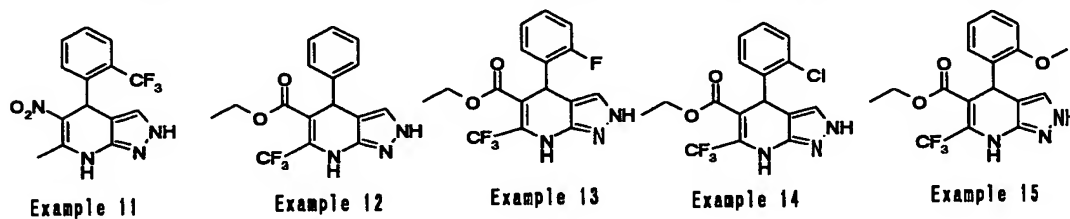
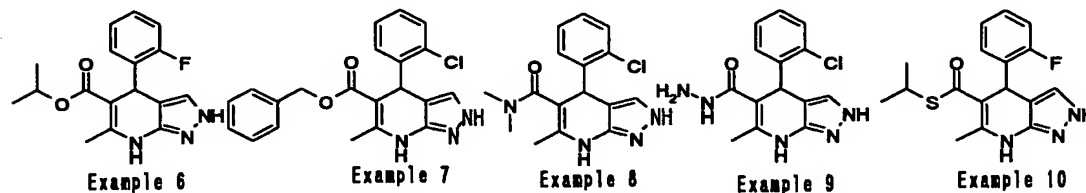
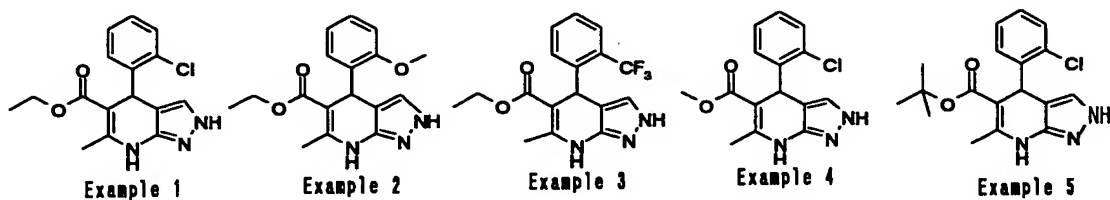
Found: C, 65.07; H, 5.05; N, 21.24.

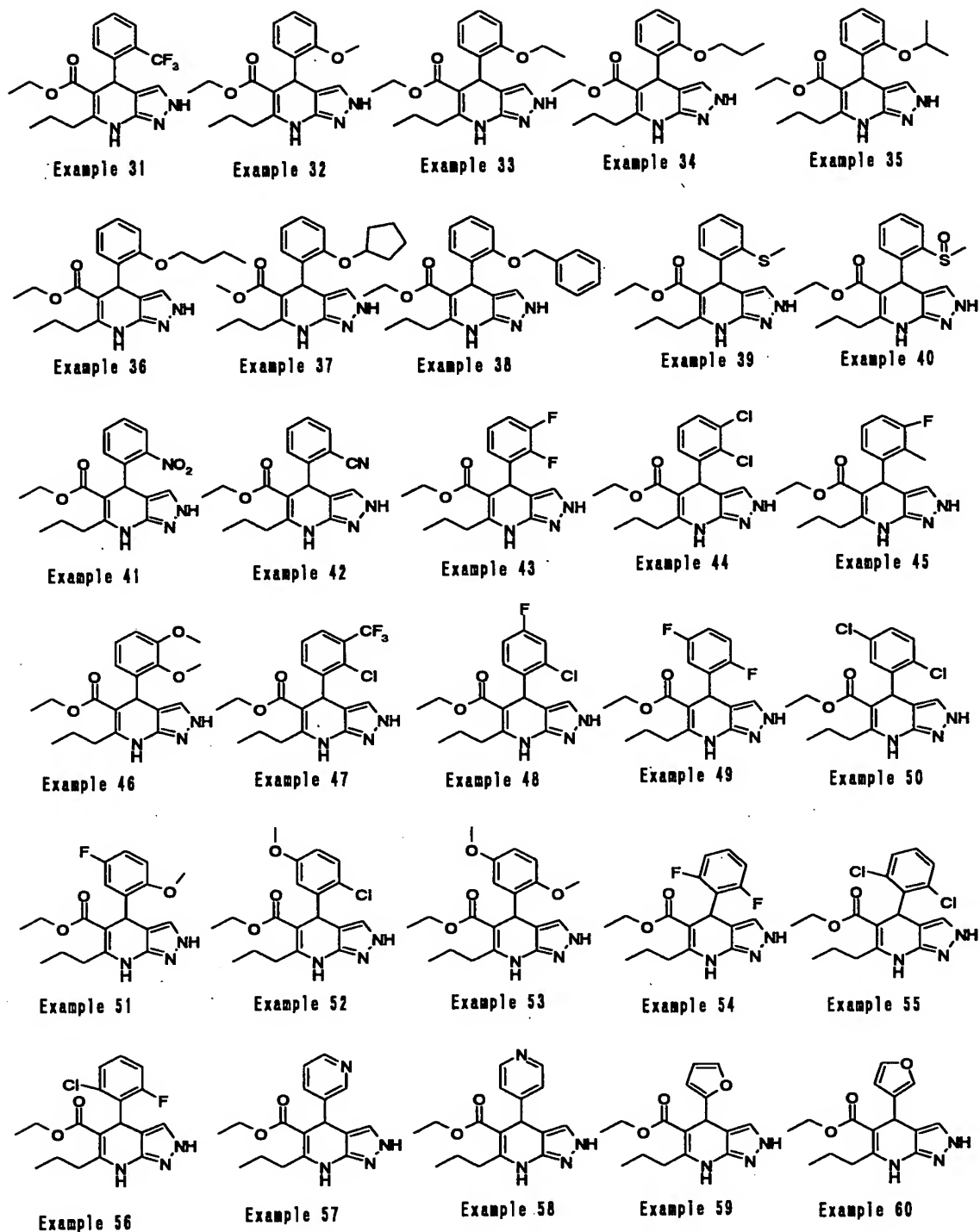
30 MS (EI): 425 (M⁺).

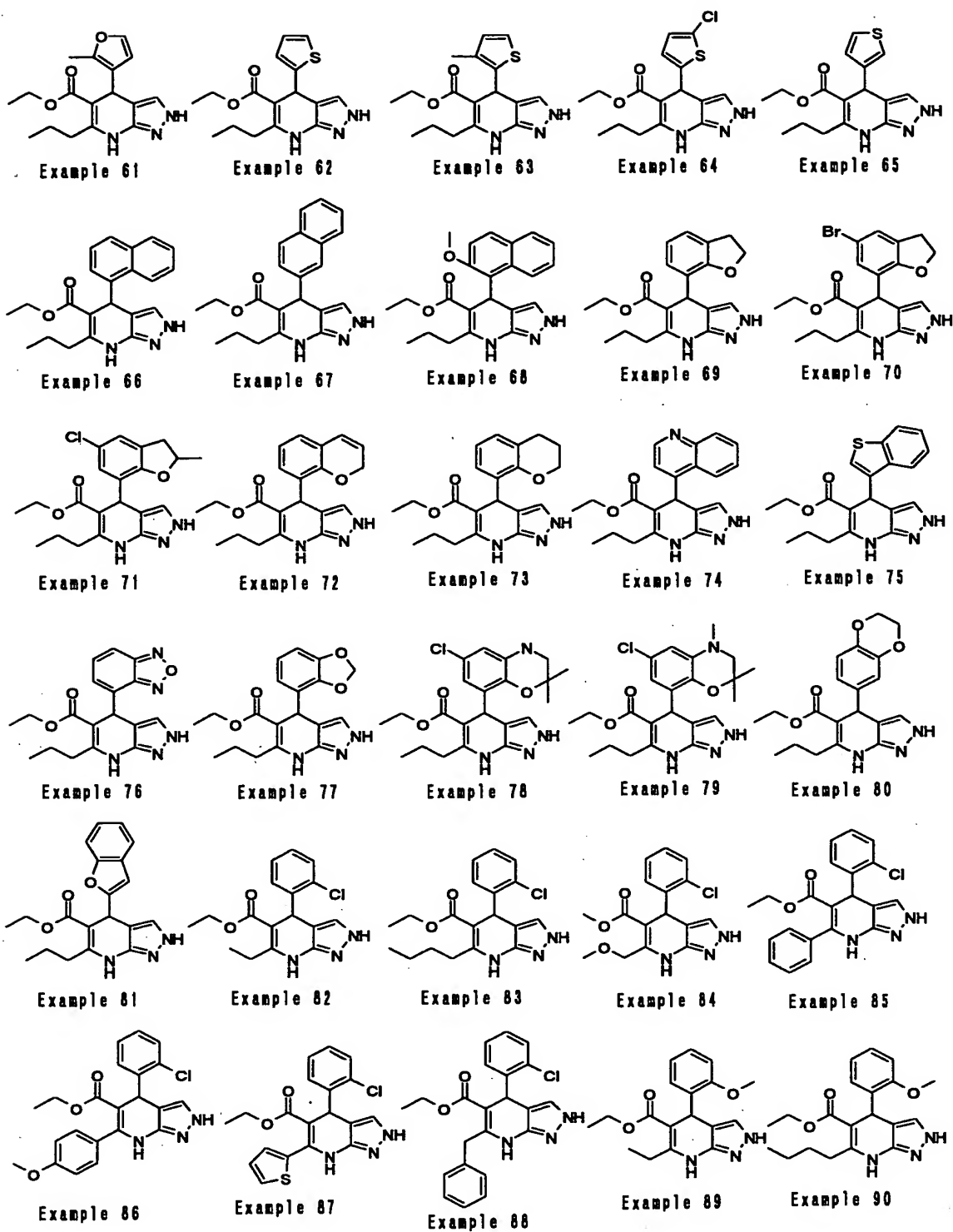
¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.91 (3H, t, J=7.3Hz), 1.62 (2H, m),
2.58 (2H, m), 5.47 (1H, s), 7.13 (1H, dd, J=6.3 and 6.6Hz), 7.32-
7.39 (3H, m), 7.49 (1H, d, J=6.5Hz), 7.61-7.91 (3H, m),

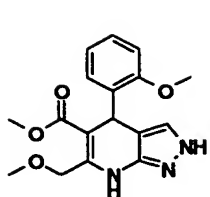
7.98 (1H, d, J=9.1Hz), 9.54 (1H, s), 10.34 (1H, s).

The compounds of the above-described Examples are as follows.

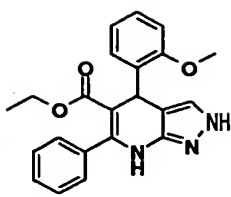




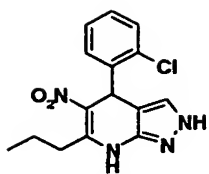




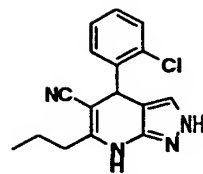
Example 91



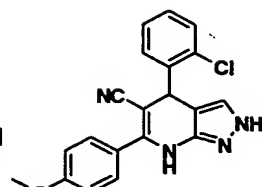
Example 92



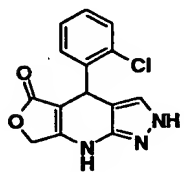
Example 93



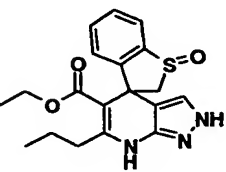
Example 94



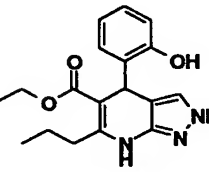
Example 95



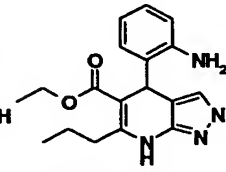
Example 96



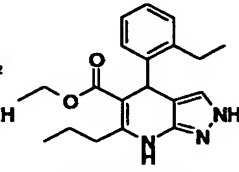
Example 97



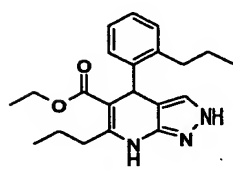
Example 98



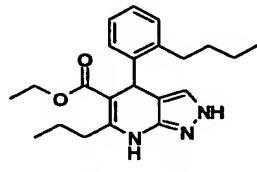
Example 99



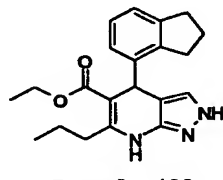
Example 100



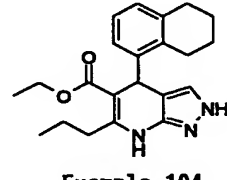
Example 101



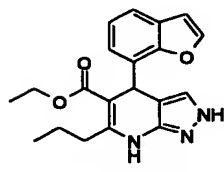
Example 102



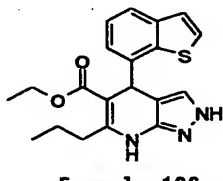
Example 103



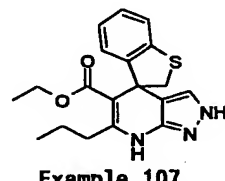
Example 104



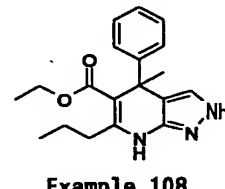
Example 105



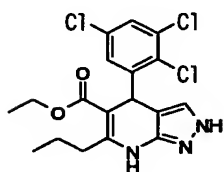
Example 106



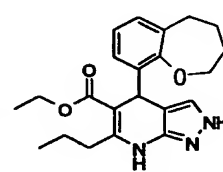
Example 107



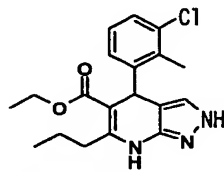
Example 108



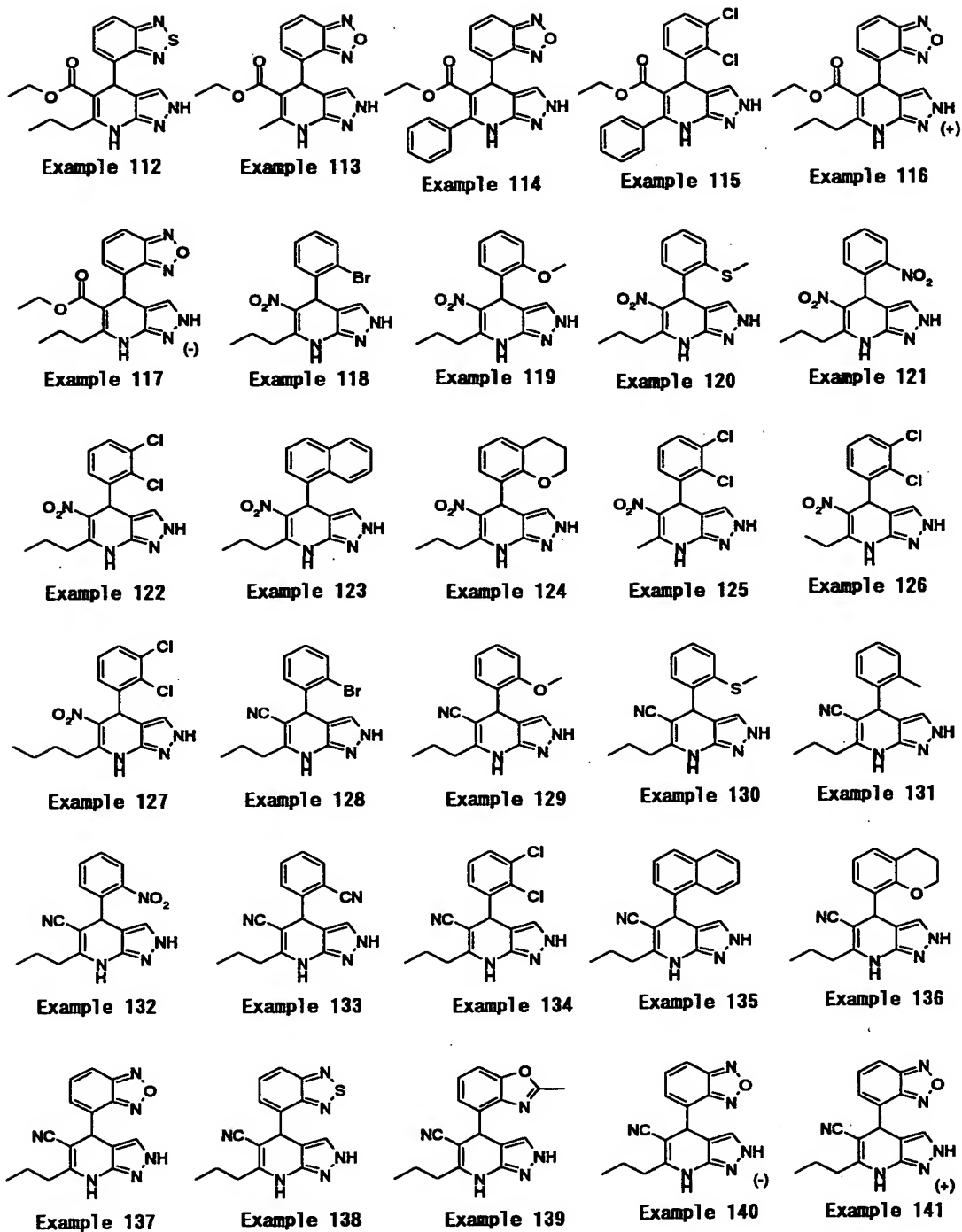
Example 109

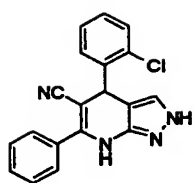


Example 110

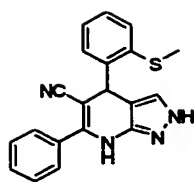


Example 111

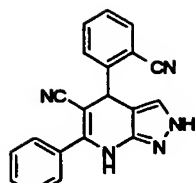




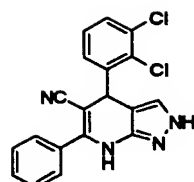
Example 142



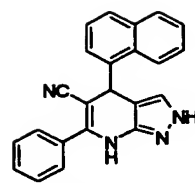
Example 143



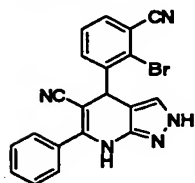
Example 144



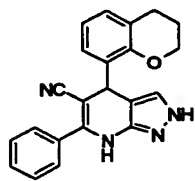
Example 145



Example 146



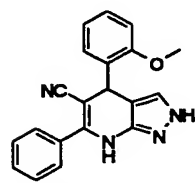
Example 147



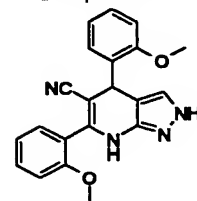
Example 148



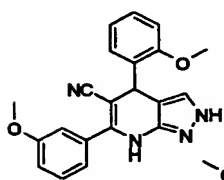
Example 149



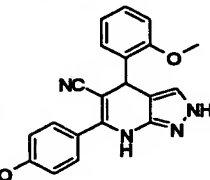
Example 150



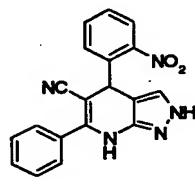
Example 151



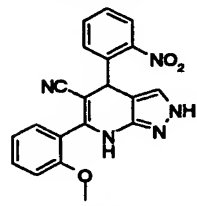
Example 152



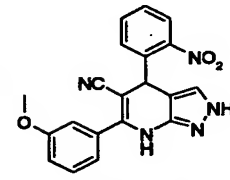
Example 153



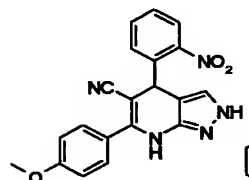
Example 154



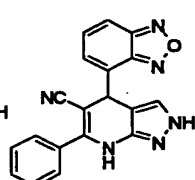
Example 155



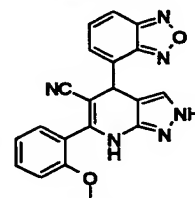
Example 156



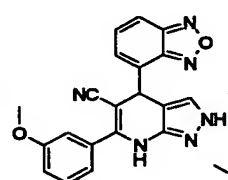
Example 157



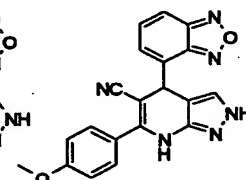
Example 158



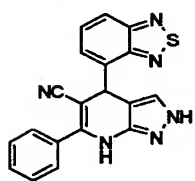
Example 159



Example 160



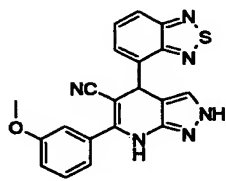
Example 161



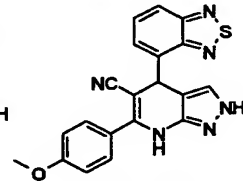
Example 162



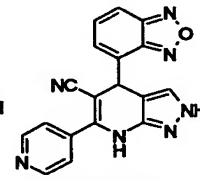
Example 163



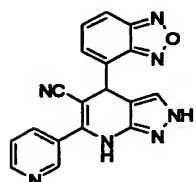
Example 164



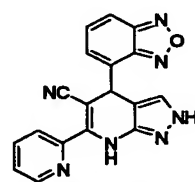
Example 165



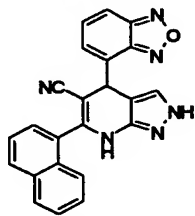
Example 166



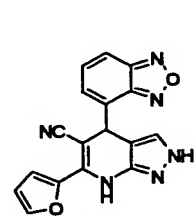
Example 167



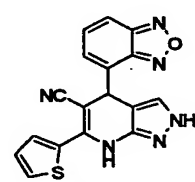
Example 168



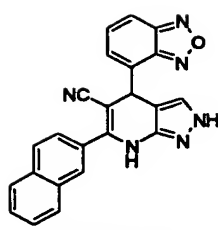
Example 169



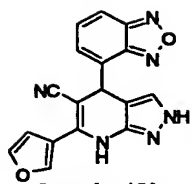
Example 170



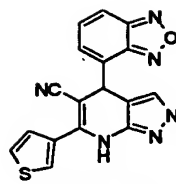
Example 171



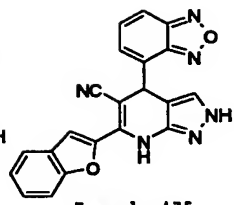
Example 172



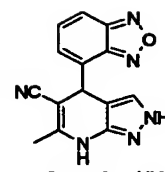
Example 173



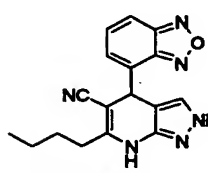
Example 174



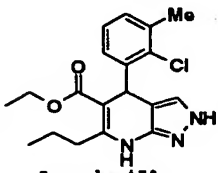
Example 175



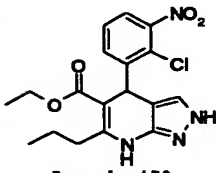
Example 176



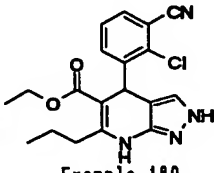
Example 177



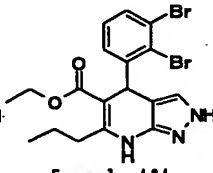
Example 178



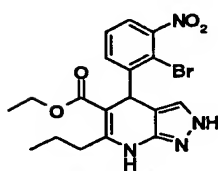
Example 179



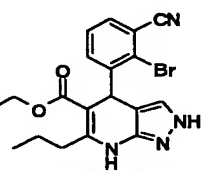
Example 180



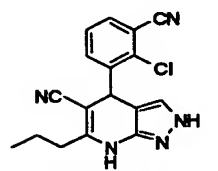
Example 181



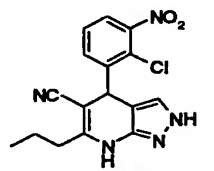
Example 182



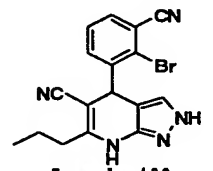
Example 183



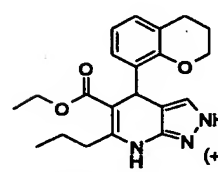
Example 184



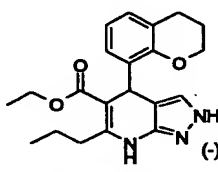
Example 185



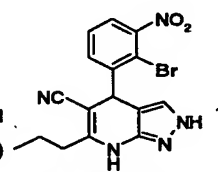
Example 186



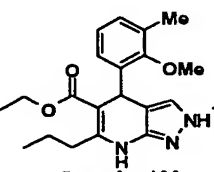
Example 187



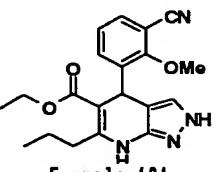
Example 188



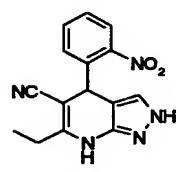
Example 189



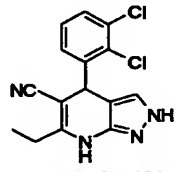
Example 190



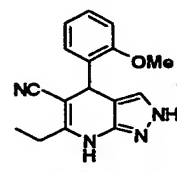
Example 191



Example 192



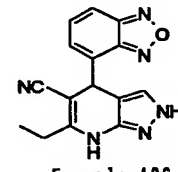
Example 193



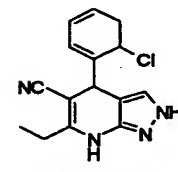
Example 194



Example 195



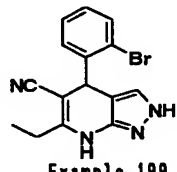
Example 196



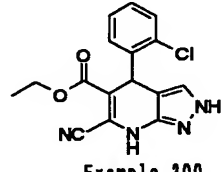
Example 197



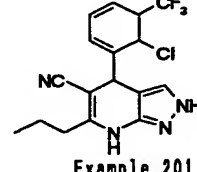
Example 198



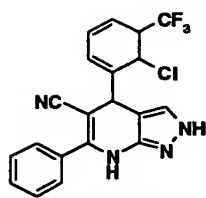
Example 199



Example 200



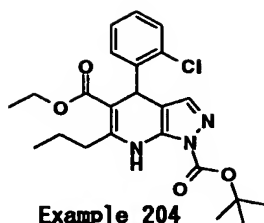
Example 201



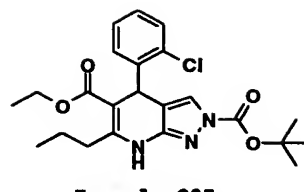
Example 202



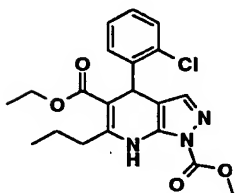
Example 203



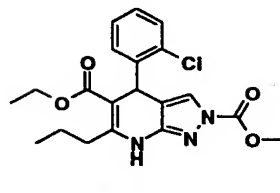
Example 204



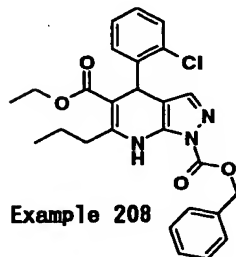
Example 205



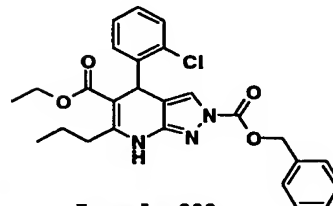
Example 206



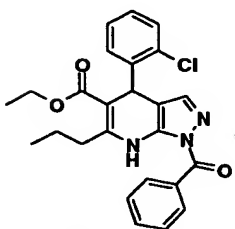
Example 207



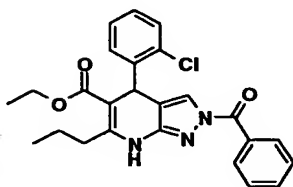
Example 208



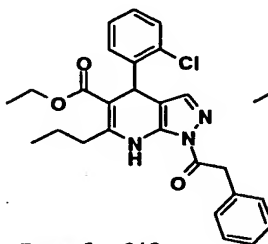
Example 209



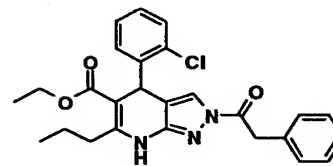
Example 210



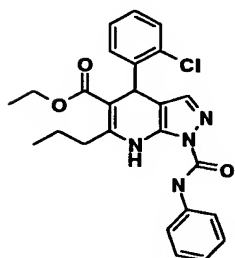
Example 211



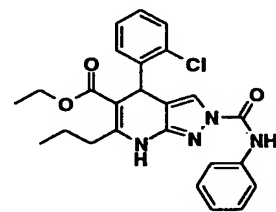
Example 212



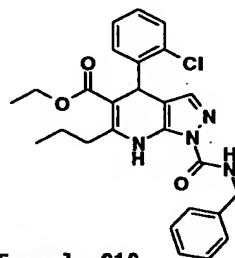
Example 213



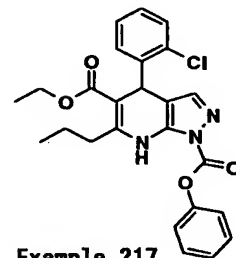
Example 214



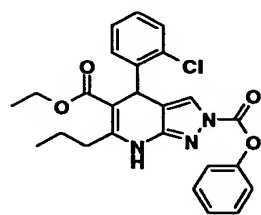
Example 215



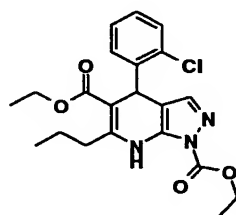
Example 216



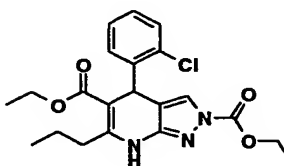
Example 217



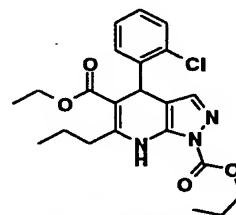
Example 218



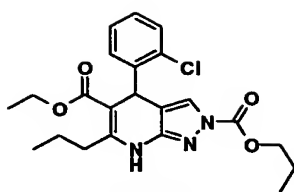
Example 219



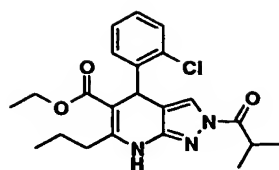
Example 220



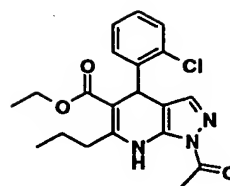
Example 221



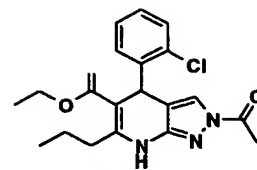
Example 222



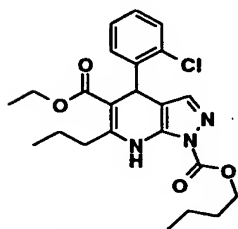
Example 223



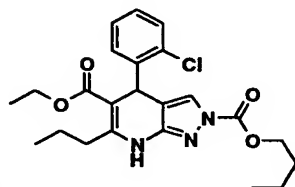
Example 224



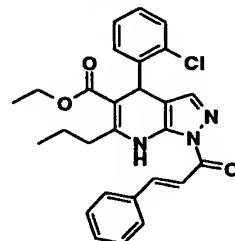
Example 225



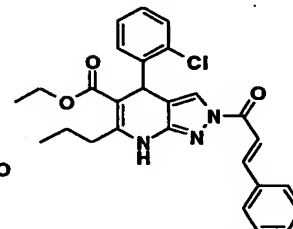
Example 226



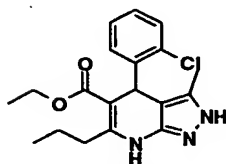
Example 227



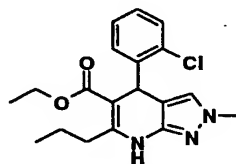
Example 228



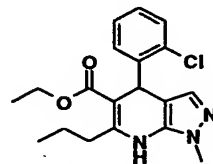
Example 229



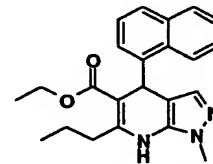
Example 230



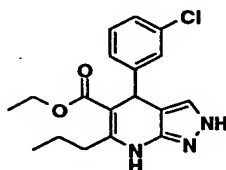
Example 231



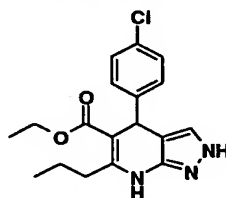
Example 232



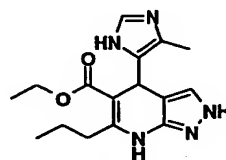
Example 233



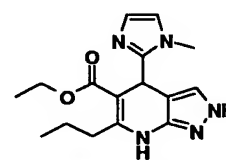
Example 234



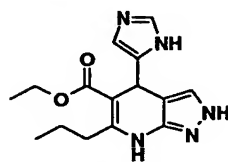
Example 235



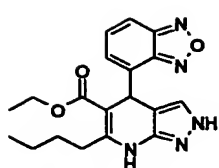
Example 236



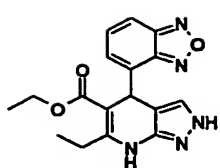
Example 237



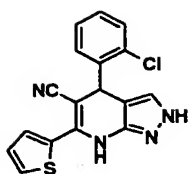
Example 238



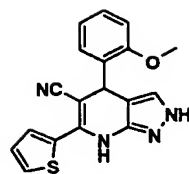
Example 239



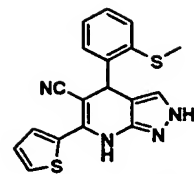
Example 240



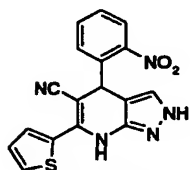
Example 241



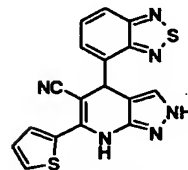
Example 242



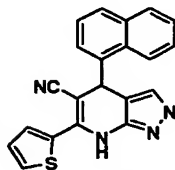
Example 243



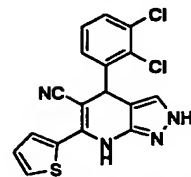
Example 244



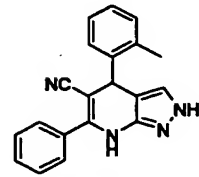
Example 245



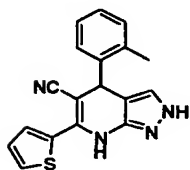
Example 246



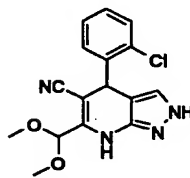
Example 247



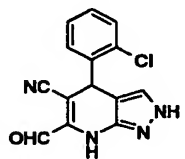
Example 248



Example 249



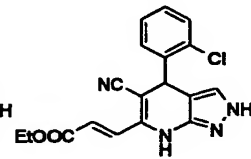
Example 250



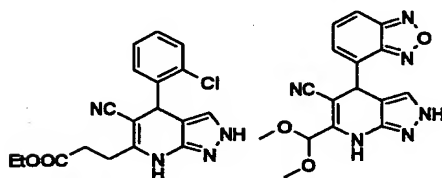
Example 251



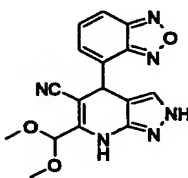
Example 252



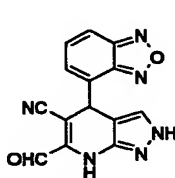
Example 253



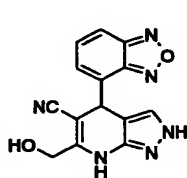
Example 254



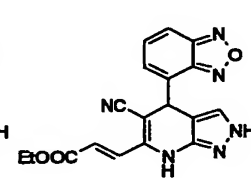
Example 255



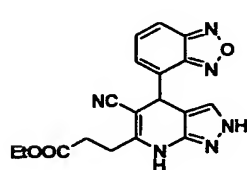
Example 256



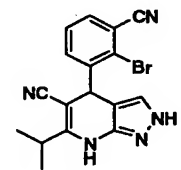
Example 257



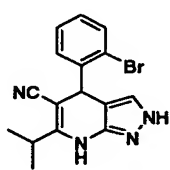
Example 258



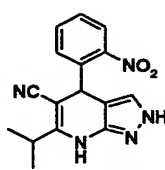
Example 259



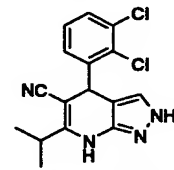
Example 260



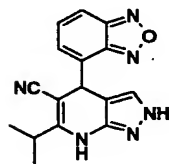
Example 261



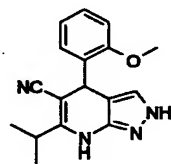
Example 262



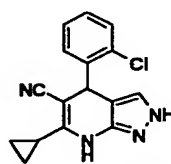
Example 263



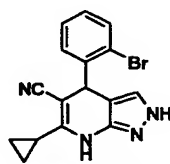
Example 264



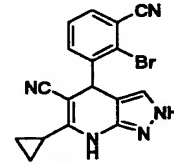
Example 265



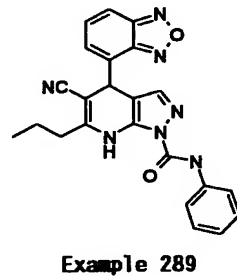
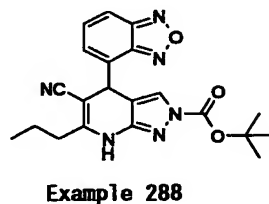
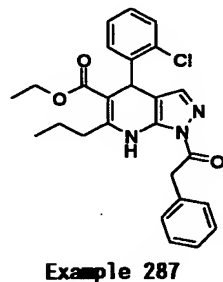
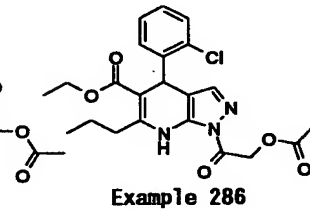
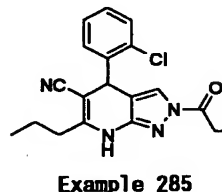
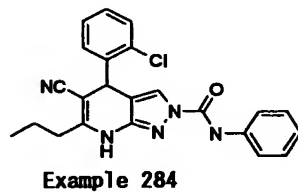
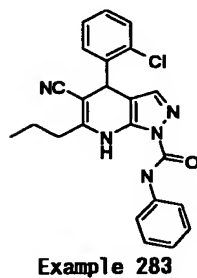
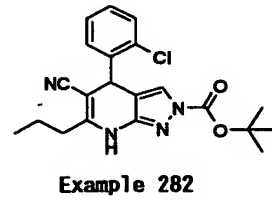
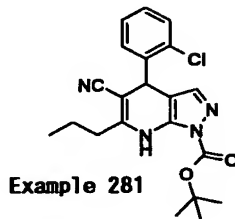
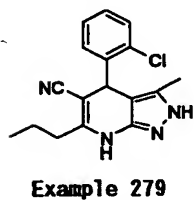
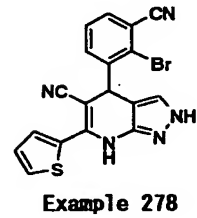
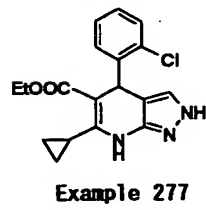
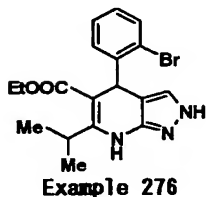
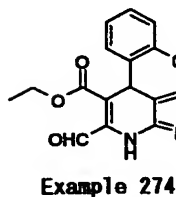
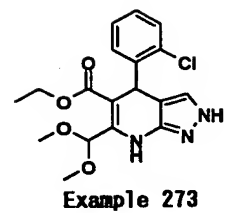
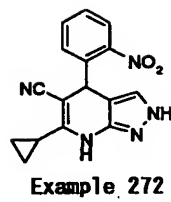
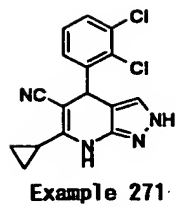
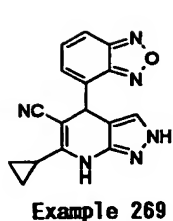
Example 266



Example 267



Example 268



Example 290

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(4-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (15 g) in DMSO (25 mL) was
5 added methyl p-anisate (25 g) and the mixture was stirred with
heating at 60°C for 1 hour. The reaction mixture was allowed
to cool and cold water (100 mL) was added dropwise. The
mixture was acidified with hydrochloric acid and the
precipitated crystals were collected by filtration. The
10 obtained crystals were extracted with ethyl acetate and the
solvent was evaporated under reduced pressure. The residue was
recrystallized from ethyl acetate to give 4-
methoxybenzoylacetonitrile (21 g) as colorless crystals. To a
solution of the obtained crystals in toluene was added
15 hydrazine monohydrate (13 g) and the mixture was heated under
reflux for 3 hours. The mixture was cooled and the
precipitated crystals were collected by filtration to give 5-
amino-3-(4-methoxyphenyl)pyrazole (22 g). Subsequently, the
title compound was prepared from methyl butyrate, 2-
20 chlorobenzaldehyde and 5-amino-3-(4-methoxyphenyl)pyrazole in
the same manner as in Example 94.

MP: 284°C.

Anal. Calcd. for: $C_{23}H_{21}ClN_4O$: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.17; H, 5.29; N, 13.86.

25 MS (EI): 404 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.3$ Hz), 1.58-
1.63 (2H, m), 2.32-2.38 (2H, m), 3.70 (3H, s), 5.56 (1H, s),
6.81 (2H, d, $J=7.2$ Hz), 7.09-7.12 (2H, m), 7.17 (1H, dd, $J=7.3$ Hz and
7.2Hz), 7.24-7.30 (3H, m), 9.85 (1H, brs), 12.46 (1H, brs).

30 Example 291

4-(2,1,3-Benzoxadiazol-4-yl)-6-(2-bromothiophen-5-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 5-

bromothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:208°C.

Anal. Calcd. for: $C_{17}H_9BrN_6OS$: C, 48.01; H, 2.13; N, 19.76.

5 Found: C, 47.94; H, 2.36; N, 19.78.

MS (EI) : 425 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54 (1H, s), 7.32-7.34 (2H, m), 7.42 (1H, d, J=3.9Hz), 7.50 (1H, d, J=6.6Hz), 7.61 (1H, dd, J=9.0Hz), 7.95 (1H, d, J=9.0Hz), 10.32 (1H, brs), 12.32 (1H, brs).

10 **Example 292**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methylthiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3-methylthiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

15 MP:202°C.

Anal. Calcd. for: $C_{18}H_{12}N_6OS$: C, 59.99; H, 3.36; N, 23.32.

Found: C, 59.89; H, 3.53; N, 23.06.

MS (EI) : 360 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.17 (3H, s), 5.54 (1H, s), 6.96 (1H, d, J=5.1Hz), 7.32 (1H, s), 7.49 (1H, d, J=6.6Hz), 7.60-7.64 (2H, m), 7.96 (1H, d, J=9.0Hz), 10.19 (1H, brs), 12.25 (1H, brs).

Example 293

25 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methoxymethylindol-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-methoxymethylindol-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

30 MP:200°C.

MS (EI) : 423 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.19 (3H, s), 5.55-5.63 (3H, m), 7.15 (1H, dd, J=7.3Hz and 7.2Hz), 7.25 (1H, dd, J=7.3Hz and 7.2Hz),

7.34 (1H, s), 7.54 (1H, d, J=7.3Hz), 7.60-7.66 (3H, m), 7.93-7.97 (2H, m), 10.12 (1H, brs), 12.22 (1H, brs).

Example 294

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-3-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:256°C.

10 Anal. Calcd. for: C₂₀H₁₇ClN₄S: C, 63.07; H, 4.50; N, 14.71.

Found: C, 62.98; H, 4.52; N, 14.68.

MS (EI): 380 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.86 (3H, t, J=7.3Hz), 1.56-1.62 (2H, m), 2.31-2.36 (2H, m), 5.46 (1H, s), 7.00-7.24 (5H, m),
15 7.36 (1H, d, J=7.3Hz), 7.50 (1H, d, J=4.9Hz), 9.95 (1H, brs),
12.74 (1H, brs).

Example 295

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(furan-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl furan-2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:253°C.

Anal. Calcd. for: C₂₀H₁₇ClN₄O: C, 65.84; H, 4.70; N, 15.36.

25 Found: C, 65.81; H, 4.84; N, 15.49.

MS (EI): 364 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88 (3H, t, J=7.3Hz), 1.58-1.63 (2H, m), 2.32-2.36 (2H, m), 5.48 (1H, s), 6.31 (1H, d, J=3.2Hz),
6.45 (1H, d, J=1.5Hz), 7.14-7.23 (3H, m), 7.36 (1H, d, J=7.3Hz),
30 7.59 (1H, s), 9.93 (1H, brs), 12.76 (1H, brs).

Example 296

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-methoxybenzoate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:>270°C.

5 Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.23; H, 5.31; N, 13.87.

MS (EI): 404 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.90 (3H, t, J=7.3Hz), 1.60-1.65 (2H, m), 2.32-2.36 (2H, m), 3.70 (3H, s), 5.41 (1H, s),
10 6.76 (1H, dd, J=7.3Hz and 7.2Hz), 6.90-6.94 (2H, m), 6.98-7.04 (2H, m), 7.08-7.15 (2H, m), 7.22 (1H, dd, J=7.3Hz and 7.2Hz), 9.83 (1H, brs), 12.21 (1H, brs).

Example 297

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(3-methoxyphenyl)-6-
15 propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3-methoxybenzoate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:239°C.

20 Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.16; H, 5.31; N, 13.80.

MS (EI): 404 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.88 (3H, t, J=7.3Hz), 1.58-1.63 (2H, m), 2.31-2.36 (2H, m), 3.68 (3H, s), 6.78 (1H, d, J=7.3Hz),
25 6.87-6.89 (2H, m), 7.11-7.20 (4H, m), 7.29 (1H, d, J=7.3Hz), 9.92 (1H, brs), 12.64 (1H, brs).

Example 298

4-(2,1,3-Benzoxadiazol-4-yl)-6-(2-chlorothiophen-5-yl)-5-
cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl 5-chlorothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:210°C.

Anal. Calcd. for: $C_{17}H_9ClN_6OS$: C, 53.62; H, 2.38; N, 22.07.

Found: C, 53.51; H, 2.67; N, 22.13.

MS (EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54 (1H, s), 7.23 (1H, d, $J=3.9$ Hz),
5 7.33 (1H, s), 7.46 (1H, d, $J=3.9$ Hz), 7.50 (1H, d, $J=6.6$ Hz),
7.60 (1H, dd, $J=9.0$ Hz and 6.6Hz), 7.95 (1H, d, $J=9.0$ Hz),
10.31 (1H, brs), 12.30 (1H, brs).

Example 299

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
10 methylthiophen-5-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 5-methylthiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 192°C.

15 MS (EI): 360 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.50 (3H, s), 5.52 (1H, s),
6.87 (1H, d, $J=3.6$ Hz), 7.32 (1H, s), 7.40 (1H, d, $J=3.7$ Hz),
7.48 (1H, d, $J=6.6$ Hz), 7.61 (1H, dd, $J=9.0$ Hz and 6.6Hz),
7.95 (1H, d, $J=9.0$ Hz), 10.12 (1H, brs), 12.26 (1H, brs).

20 Example 300

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(naphthalen-1-yl)-6-
propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl naphthalene-1-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the
25 same manner as in Example 290.

MP: 254°C.

Anal. Calcd. for: $C_{26}H_{21}ClN_4$: C, 73.49; H, 4.98; N, 13.19.

Found: C, 73.81; H, 5.05; N, 13.08.

MS (EI): 424 (M^+).

30 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, $J=7.3$ Hz), 1.64-
1.70 (2H, m), 2.46-2.49 (2H, m), 5.25 (1H, s), 6.88-7.02 (5H, m),
7.31 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.42-7.47 (3H, m), 7.83-
7.88 (2H, m), 9.95 (1H, brs), 12.46 (1H, brs).

Example 301

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(naphthalen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl naphthalene-
5 2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the
same manner as in Example 290.

MP: >270°C.

Anal. Calcd. for: C₂₆H₂₁ClN₄: C, 73.49; H, 4.98; N, 13.19.

Found: C, 73.23; H, 5.01; N, 13.26.

10 MS (EI): 424 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.91 (3H, t, J=7.3Hz), 1.61-
1.66 (2H, m), 2.31-2.41 (2H, m), 5.76 (1H, s), 7.05 (1H, dd, J=7.3Hz
and 7.2Hz), 7.12-7.16 (2H, m), 7.28 (1H, d, J=7.3Hz), 7.45-
7.52 (2H, m), 7.57 (1H, d, J=7.3Hz), 7.77-7.84 (4H, m), 9.94 (1H, brs),
15 12.79 (1H, brs) .

Example 302

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3,6-dipropyl-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (4.8 g) in THF (150 mL)
20 was added n-BuLi (67 mmol) at -78°C. Methyl butyrate (10 g)
was added and the mixture was stirred for 1 hour. The reaction
mixture was acidified with hydrochloric acid and extracted
with ethyl acetate. The solvent was evaporated under reduced
pressure and the residue was purified by silica gel column
25 chromatography (eluent: hexane-ethyl acetate (10:1)) to give
1-cyanopentan-2-one (5.5 g) as a colorless oil. To a solution
of the obtained colorless oil in toluene was added hydrazine
monohydrate (5.0 g) and the mixture was heated under reflux
for 3 hours. The mixture was cooled and the solvent was
30 evaporated under reduced pressure. The reaction mixture was
purified by silica gel column chromatography (eluent:
chloroform-methanol (10:1)) to give 5-amino-3-propylpyrazole
(5.0 g). A solution of 2-chloroaldehyde (1.7 g), 5-amino-3-

propylpyrazole (1.5 g) and 1-cyanopentan-2-one (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The mixture was cooled to room temperature and the precipitated crystals were collected by filtration to give the title
5 compound (2.1 g) as colorless crystals.

MP:237°C.

Anal. Calcd. for: $C_{19}H_{21}ClN_4$: C, 66.95; H, 6.21; N, 16.44.

Found: C, 66.98; H, 6.26; N, 16.41.

MS(EI): 340 (M^+).

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.57 (3H, t, $J=7.3$ Hz),
0.91 (3H, t, $J=7.3$ Hz), 1.02-1.07 (2H, m), 1.59-1.65 (2H, m), 2.01-
2.12 (2H, m), 2.30-2.38 (2H, m), 5.28 (1H, s), 7.20-7.23 (2H, m),
7.30 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.38 (1H, d, $J=7.3$ Hz),
9.70 (1H, brs), 11.85 (1H, brs).

15 **Example 303**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-hydroxy-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 2-chlorobenzaldehyde and 3-amino-5-hydroxypyrazole in the same
20 manner as in Example 94.

MS(EI): 314 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89 (3H, t, $J=7.3$ Hz), 1.56-
1.60 (2H, m), 2.26-2.38 (2H, m), 5.11 (1H, s), 7.14-7.21 (3H, m),
7.27 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.34 (1H, d, $J=7.3$ Hz),
25 9.64 (1H, brs), 10.45 (1H, brs).

Example 304

3-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pentanoate,
30 methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:212°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4$: C, 67.69; H, 6.53; N, 15.79.

Found: C, 67.58; H, 6.46; N, 15.75.

MS (EI): 354 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.64 (3H, t, $J=7.3\text{Hz}$), 0.89-
0.98 (6H, m), 1.10-1.14 (1H, m), 1.59-1.64 (2H, m), 2.05-2.16 (2H, m),
5 2.31-2.35 (2H, m), 5.28 (1H, s), 7.20-7.24 (2H, m),
7.29 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.38 (1H, d, $J=7.3\text{Hz}$),
9.70 (1H, brs), 11.85 (1H, brs).

Example 305

4-(2,1,3-Benzoxadiazol-4-yl)-6-(benzothiophen-2-yl)-5-cyano-
10 4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
benzothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde
and 3-aminopyrazole in the same manner as in Example 95.

MP: 220°C.

15 Anal. Calcd. for: $\text{C}_{21}\text{H}_{12}\text{N}_6\text{OS}$: C, 63.62; H, 3.05; N, 21.20.

Found: C, 63.58; H, 3.29; N, 21.09.

MS (EI): 396 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 5.60 (1H, s), 7.36 (1H, s), 7.44-
7.46 (2H, m), 7.54 (1H, d, $J=6.3\text{Hz}$), 7.64 (1H, dd, $J=9.0\text{Hz}$ and 6.6Hz),
20 7.88 (1H, s), 7.94-7.98 (2H, m), 8.05 (1H, d, $J=9.0\text{Hz}$), 10.40 (1H, brs),
12.31 (1H, brs).

Example 306

4-(2-Chlorophenyl)-5-cyano-6-cyclohexyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl
cyclohexanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 163°C.

Anal. Calcd. for: $\text{C}_{19}\text{H}_{19}\text{ClN}_4 \cdot \frac{1}{2} \text{H}_2\text{O}$: C, 65.61; H, 5.80; N, 16.11.

30 Found: C, 65.40; H, 5.77; N, 15.86.

MS (EI): 338 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.16-1.30 (3H, m), 1.66-1.85 (7H, m),
2.66-2.72 (1H, m), 5.33 (1H, s), 7.21-7.25 (3H, m),

7.32 (1H, dd, J=7.3Hz and 7.2Hz), 7.41 (1H, d, J=7.3Hz),
9.60 (1H, brs), 12.15 (1H, brs).

Example 307

6-t-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo
5 [3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 198°C.

10 Anal. Calcd. for: C₁₇H₁₇ClN₄: C, 65.28; H, 5.48; N, 17.91.

Found: C, 64.98; H, 5.47; N, 17.78.

MS (EI): 312 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.41 (9H, s), 5.33 (1H, s), 7.21-
7.33 (4H, m), 7.41 (1H, d, J=7.3Hz), 8.88 (1H, brs), 12.20 (1H, brs).

15 **Example 308**

4-(2-Chlorophenyl)-5-cyano-3-cyclopropyl-4,7-dihydro-6-propyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cyclopropanecarboxylate, methyl butyrate and 2-
20 chlorobenzaldehyde in the same manner as in Example 302.

MP: 270°C.

Anal. Calcd. for: C₁₉H₁₉ClN₄: C, 67.35; H, 5.65; N, 16.54.

Found: C, 67.34; H, 5.66; N, 16.62.

MS (EI): 338 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.22-0.25 (1H, m), 0.41-0.44 (1H, m),
0.50-0.54 (1H, m), 0.62-0.66 (1H, m), 0.90 (3H, t, J=7.3Hz), 1.25-
1.29 (1H, m), 1.58-1.63 (2H, m), 2.31-2.36 (2H, m), 5.33 (1H, s), 7.18-
7.23 (2H, m), 7.30 (1H, dd, J=7.3Hz and 7.2Hz), 7.38 (1H, d, J=7.3Hz),
9.69 (1H, brs), 11.73 (1H, brs).

30 **Example 309**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-ethyl-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate,

methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:269°C.

Anal. Calcd. for: $C_{18}H_{19}ClN_4$: C, 66.15; H, 5.86; N, 17.14.

5 Found: C, 66.27; H, 5.86; N, 17.25.

MS (EI): 326 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.72 (3H, t, $J=7.3$ Hz),
0.91 (3H, t, $J=7.3$ Hz), 1.59-1.64 (2H, m), 2.09-2.11 (2H, m), 2.31-
2.40 (2H, m), 5.29 (1H, s), 7.20-7.24 (2H, m), 7.30 (1H, dd, $J=7.3$ Hz
10 and 7.2Hz), 7.38 (1H, d, $J=7.3$ Hz), 9.70 (1H, brs), 11.86 (1H, brs).

Example 310

3-t-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate,
15 methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4$: C, 67.69; H, 6.53; N, 15.79.

Found: C, 67.55; H, 6.56; N, 15.66.

20 MS (EI): 354 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.84 (3H, t, $J=7.3$ Hz), 0.95 (9H, s),
1.53-1.59 (2H, m), 2.26-2.30 (2H, m), 5.39 (1H, s),
6.97 (1H, d, $J=7.3$ Hz), 7.20 (1H, dd, $J=7.3$ Hz and 7.2Hz),
7.27 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.38 (1H, d, $J=7.3$ Hz),
25 9.73 (1H, brs), 11.87 (1H, brs).

Example 311

4-(2-Chlorophenyl)-5-cyano-3-cyclohexyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
30 cyclohexanecarboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

Anal. Calcd. for: $C_{22}H_{25}ClN_4$: C, 69.37; H, 6.62; N, 14.71.

Found: C, 69.17; H, 6.62; N, 14.91.

MS (EI): 380 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.89-1.17 (9H, m), 1.47-1.64 (6H, m),
2.06-2.08 (1H, m), 2.31-2.38 (2H, m), 5.30 (1H, s), 7.19-7.23 (2H, m),
5 7.29 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.38 (1H, d, $J=7.3\text{Hz}$),
9.71 (1H, brs), 11.83 (1H, brs).

Example 312

4-(2-Chlorophenyl)-5-cyano-6-cycloheptyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl cycloheptanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 146°C.

MS (EI): 352 (M^+).

15 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.42-1.98 (12H, m), 2.78-2.81 (1H, m), 5.33 (1H, s), 7.21-7.24 (3H, m), 7.32 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.41 (1H, d, $J=7.3\text{Hz}$), 9.61 (1H, brs), 12.18 (1H, brs).

Example 313

20 4-(2-Chlorophenyl)-5-cyano-6-cyclobutyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclobutanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 188°C.

25 Anal. Calcd. for: $\text{C}_{17}\text{H}_{15}\text{ClN}_4$: C, 65.70; H, 4.86; N, 18.03.

Found: C, 65.51; H, 5.21; N, 18.27.

MS (EI): 310 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.72-1.77 (1H, m), 1.93-1.97 (1H, m),
2.09-2.12 (2H, m), 2.38-2.43 (2H, m), 2.58-2.61 (1H, m), 5.33 (1H, s),
30 7.20-7.32 (4H, m), 7.41 (1H, d, $J=7.3\text{Hz}$), 9.72 (1H, brs),
12.18 (1H, brs).

Example 314

4-(2-Chlorophenyl)-5-cyano-3-cyclopentyl-4,7-dihydro-6-propyl-

2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

5 MP:>270°C.

Anal. Calcd. for: C₂₁H₂₃ClN₄: C, 68.75; H, 6.32; N, 15.27.

Found: C, 68.56; H, 6.36; N, 15.22.

MS (EI): 366 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.89 (3H, t, J=7.3Hz), 1.31-
10 1.74 (10H, m), 2.30-2.37 (2H, m), 2.52-2.54 (1H, m),
5.30 (1H, s), 7.17-7.22 (2H, m), 7.28 (1H, dd, J=7.3Hz and 7.2Hz),
7.37 (1H, d, J=7.3Hz), 9.71 (1H, brs), 11.86 (1H, brs).

Example 315

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-3-isopropyl-

15 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-methylpropionate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

20 Anal. Calcd. for: C₁₉H₂₁ClN₄: C, 66.95; H, 6.21; N, 16.44.

Found: C, 66.90; H, 6.27; N, 16.44.

MS (EI): 340 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.67 (3H, d, J=7.2Hz),
0.90 (3H, t, J=7.3Hz), 0.95 (3H, d, J=7.3Hz), 1.57-1.63 (2H, m), 2.30-
25 2.35 (2H, m), 5.30 (1H, s), 7.19-7.23 (2H, m), 7.29 (1H, dd, J=7.3Hz
and 7.2Hz), 7.38 (1H, d, J=7.3Hz), 9.71 (1H, brs), 11.88 (1H, brs).

Example 316

4-(2-Chlorophenyl)-5-cyano-6-cyclopentyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl cyclopentanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:225°C.

Anal. Calcd. for: $C_{18}H_{17}ClN_4 \cdot 1/5 H_2O$: C, 65.83; H, 5.34; N, 17.06.

Found: C, 66.02; H, 5.51; N, 16.62.

MS (EI): 324 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.56-1.60 (2H, m), 1.78-1.87 (6H, m),
5 3.06-3.10 (1H, m), 5.34 (1H, s), 7.22-7.26 (3H, m),
7.32 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.42 (1H, d, $J=7.3$ Hz),
9.61 (1H, brs), 12.16 (1H, brs).

Example 317

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclopentyl-4,7-dihydro-
10 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 247°C.

15 MS (EI): 394 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.52-1.58 (2H, m), 1.75-1.82 (6H, m),
3.01-3.06 (1H, m), 5.46 (1H, s), 7.33 (1H, s), 7.54-7.58 (2H, m),
7.84 (1H, d, $J=7.3$ Hz), 9.73 (1H, brs), 12.25 (1H, brs).

Example 318

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclopentyl-4,7-
20 dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

25 MP: 193°C.

Anal. Calcd. for: $C_{18}H_{16}N_6O$: C, 65.05; H, 4.85; N, 25.29.

Found: C, 64.72; H, 4.98; N, 24.86.

MS (EI): 332 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.55-1.58 (2H, m), 1.80-1.86 (6H, m),
30 3.06-3.09 (1H, m), 5.39 (1H, s), 7.26 (1H, s), 7.38 (1H, d, $J=6.6$ Hz),
7.60 (1H, dd, $J=9.0$ Hz and 6.6Hz), 7.91 (1H, d, $J=9.0$ Hz),
9.72 (1H, brs), 12.15 (1H, brs).

Example 319

4-(2-Bromo-3-cyanophenyl)-6-t-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:251°C.

Anal. Calcd. for: $C_{18}H_{16}BrN_5 \cdot \frac{1}{2} H_2O$: C, 55.25; H, 4.38; N, 17.90.

Found: C, 55.55; H, 4.30; N, 18.14.

10 MS (EI) : 382 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.41 (9H, s), 5.46 (1H, s), 7.33 (1H, s), 7.54-7.60 (2H, m), 7.82 (1H, d, J=7.3Hz), 9.00 (1H, brs), 12.29 (1H, brs).

Example 320

15 4-(2,1,3-Benzoxadiazol-4-yl)-6-t-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

20 MP:204°C.

Anal. Calcd. for: $C_{17}H_{16}N_6O \cdot \frac{1}{2} H_2O$: C, 63.03; H, 5.10; N, 25.94.

Found: C, 63.08; H, 5.08; N, 26.00.

MS (EI) : 320 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.40 (9H, s), 5.37 (1H, s), 7.26 (1H, s), 7.38 (1H, d, J=6.6Hz), 7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.91 (1H, d, J=9.0Hz), 9.02 (1H, brs), 12.20 (1H, brs).

Example 321

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclobutyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl cyclobutanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:278°C.

Anal. Calcd. for: $C_{18}H_{14}BrN_5$: C, 56.86; H, 3.71; N, 18.42.

Found: C, 56.57; H, 3.79; N, 18.48.

MS (EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.71 (1H, m), 1.88-1.95 (1H, m),
5 2.06-2.13 (2H, m), 2.38-2.47 (2H, m), 3.56-3.60 (1H, m), 5.45 (1H, s),
7.33 (1H, s), 7.57-7.59 (2H, m), 7.82 (1H, d, $J=7.3$ Hz), 9.84 (1H, brs),
12.27 (1H, brs).

Example 322

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclobutyl-4,7-dihydro-
10 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclobutanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 194°C.

15 Anal. Calcd. for: $C_{17}H_{14}N_6O$: C, 64.14; H, 4.43; N, 26.40.

Found: C, 64.08; H, 4.51; N, 26.26.

MS (EI): 318 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.72-1.76 (1H, m), 1.90-1.97 (1H, m),
2.10-2.14 (2H, m), 2.39-2.46 (2H, m), 3.56-3.60 (1H, m), 5.38 (1H, s),
20 7.26 (1H, s), 7.37 (1H, d, $J=6.6$ Hz), 7.58 (1H, dd, $J=9.0$ Hz and 6.6Hz),
7.91 (1H, d, $J=9.0$ Hz), 9.82 (1H, brs), 12.17 (1H, brs).

Example 323

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclohexyl-4,7-dihydro-
25 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclohexanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 210°C.

Anal. Calcd. for: $C_{19}H_{18}N_6O$: C, 65.88; H, 5.24; N, 24.26.

30 Found: C, 65.88; H, 5.25; N, 24.19.

MS (EI): 346 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.21-1.26 (3H, m), 1.62-1.80 (7H, m),
2.66-2.70 (1H, m), 5.38 (1H, s), 7.25 (1H, s), 7.38 (1H, d, $J=6.6$ Hz),

7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.91 (1H, d, J=9.0Hz),
9.72 (1H, brs), 12.15 (1H, brs).

Example 324

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cycloheptyl-4,7-
5 dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cycloheptanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and
3-aminopyrazole in the same manner as in Example 94.

MP:228°C.

10 Anal. Calcd. for: C₂₀H₂₀N₆O:C, 66.65;H, 5.59;N, 23.32.

Found: C, 66.45;H, 5.70;N, 22.97.

MS (EI) : 360 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.38-1.98 (12H, m), 2.76-
2.79 (1H, m), 5.37 (1H, s), 7.24 (1H, s), 7.38 (1H, d, J=6.6Hz),
15 7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.91 (1H, d, J=9.0Hz), 9.72 (1H, brs),
12.13 (1H, brs).

Example 325

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclohexyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl
cyclohexanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP:193°C.

Anal. Calcd. for: C₂₀H₁₈BrN₅ 1/2 H₂O:C, 57.56;H, 4.59;N, 16.78.

25 Found: C, 57.25;H, 4.37;N, 16.56.

MS (EI) : 408 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.21-1.26 (3H, m), 1.66-1.80 (7H, m),
2.66-2.69 (1H, m), 5.45 (1H, s), 7.33 (1H, s), 7.55-7.60 (2H, m),
7.82 (1H, d, J=7.3Hz), 9.73 (1H, brs), 12.24 (1H, brs).

30 **Example 326**

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cycloheptyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cycloheptanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:252°C.

Anal. Calcd. for: $C_{21}H_{20}BrN_5 \cdot \frac{1}{2} H_2O$: C, 58.48; H, 4.91; N, 16.24.

5 Found: C, 58.53; H, 4.73; N, 16.19.

MS (EI): 422 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.44-1.58 (12H, m), 2.76-2.79 (1H, m), 5.44 (1H, s), 7.31 (1H, s), 7.54-7.60 (2H, m), 7.83 (1H, d, $J=7.3$ Hz), 9.73 (1H, brs), 12.23 (1H, brs).

10 Example 327

5-Cyano-4,7-dihydro-6-propyl-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, pyridine-3-aldehyde and 3-aminopyrazole in the same manner as
15 in Example 94.

MP:201°C.

Anal. Calcd. for: $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40.

Found: C, 67.42; H, 5.74; N, 26.72.

MS (EI): 265 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, $J=7.3$ Hz), 1.62-1.67 (2H, m), 2.36-2.39 (2H, m), 4.98 (1H, s), 7.27 (1H, s), 7.35 (1H, dd, $J=7.3$ Hz and 2.9Hz), 7.54 (1H, d, $J=7.3$ Hz), 8.41-8.44 (2H, m), 9.81 (1H, brs), 12.18 (1H, brs).

Example 328

25 3-t-Butoxycarbonyloxy-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-3-hydroxy-6-propyl-2H-pyrazolo[3,4-b]pyridine (12.5 g) in THF (400 mL) was added triethylamine (4.5 g),
30 dimethylaminopyridine (0.5 g) and di-t-butylcarbonate (9.6 g) and the mixture was stirred for 3 hours. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was recrystallized from

ethyl acetate to give the title compound (12 g) as colorless crystals.

MP:182°C.

Anal. Calcd. for: $C_{21}H_{23}ClN_4O_3$: C, 60.79; H, 5.59; N, 13.50.

5 Found: C, 60.60; H, 5.50; N, 13.44.

MS (EI): 414 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, $J=7.3$ Hz), 1.54 (9H, s),
2.49-2.51 (2H, m), 5.18 (1H, s), 7.23-7.27 (2H, m),
7.32 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.38 (1H, d, $J=7.3$ Hz),
10 9.15 (1H, brs), 10.99 (1H, brs).

Example 329

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(2,2-dimethoxyethyl)-
4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3,3-
15 dimethoxypropionate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:115°C.

Anal. Calcd. for: $C_{17}H_{16}N_6O_3 \cdot 1.0 H_2O$: C, 55.13; H, 4.90; N, 22.69.

Found: C, 55.30; H, 4.51; N, 22.99.

20 MS (EI): 352 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.71 (2.75 (2H, m), 3.28 (3H, s),
3.31 (3H, s), 4.74 (1H, t, $J=5.9$ Hz), 5.43 (1H, s), 7.28 (1H, s),
7.40 (1H, d, $J=6.6$ Hz), 7.61 (1H, dd, $J=9.0$ Hz and 6.6Hz),
7.92 (1H, d, $J=9.0$ Hz), 9.99 (1H, brs), 12.18 (1H, brs).

25 Example 330

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(2,2-dimethoxyethyl)-
6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3,3-
dimethoxypropionate, methyl butyrate and 2-chlorobenzaldehyde
30 in the same manner as in Example 302.

MP:180°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4O_2$: C, 62.09; H, 5.99; N, 14.48.

Found: C, 62.35; H, 6.02; N, 14.50.

MS (EI) : 386 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.91 (3H, t, J=7.3Hz), 1.59-
1.64 (2H, m), 2.28-2.35 (4H, m), 3.00 (3H, s), 3.02 (3H, s),
3.81 (1H, t, J=7.3Hz), 5.31 (1H, s), 7.24-7.31 (3H, m),
5 7.40 (1H, d, J=7.3Hz), 9.75 (1H, brs), 11.92 (1H, brs) .

Example 331

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate,
10 2,1-benzoisoxazole-4-aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 239°C.

MS (EI) : 305 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.91 (3H, t, J=7.3Hz), 1.64-
15 1.67 (2H, m), 2.40-2.43 (2H, m), 5.23 (1H, s), 6.91 (1H, d, J=6.6Hz),
7.28 (1H, s), 7.36 (1H, dd, J=9.3Hz and 6.6Hz), 7.52 (1H, d, J=9.3Hz),
9.37 (1H, s), 9.96 (1H, brs), 12.21 (1H, brs) .

Example 332

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
2,1-benzoisoxazole-4-aldehyde and 3-aminopyrazole in the same
manner as in Example 94:

MP: 245°C.

25 MS (EI) : 305 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.23-1.26 (6H, m),
3.03 (1H, t, J=5.9Hz), 5.21 (1H, s), 6.92 (1H, d, J=6.6Hz), 7.30 (1H, s),
7.37 (1H, dd, J=9.3Hz and 6.6Hz), 7.53 (1H, d, J=9.3Hz), 9.34 (1H, s),
9.78 (1H, brs), 12.23 (1H, brs) .

30 **Example 333**

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-6-cyclopropyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cyclopropanecarboxylate, 2,1-benzisoxazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:248°C.

MS (EI) : 303 (M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.89-0.91 (2H, m), 1.05-1.08 (2H, m), 1.94-1.98 (2H, m), 5.20 (1H, s), 6.91 (1H, d, J=6.6Hz), 7.28 (1H, s), 7.36 (1H, dd, J=9.3Hz and 6.6Hz), 7.52 (1H, d, J=9.3Hz), 9.26 (1H, s), 9.36 (1H, brs), 12.22 (1H, brs).

Example 334

10 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(1-t-butoxycarbonylindol-3-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-t-butoxycarbonylindole-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 15 95.

MP:202°C.

MS (EI) : 479 (M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.65 (9H, s), 5.60 (1H, s), 7.27-7.41 (3H, m), 7.54-7.58 (2H, m), 7.64 (1H, dd, J=7.3Hz and 7.2Hz), 7.97 (1H, d, J=7.3Hz), 8.03 (1H, s), 8.10 (1H, d, J=7.3Hz), 10.23 (1H, brs), 12.26 (1H, brs).

Example 335

25 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(indol-3-yl)-2H-pyrazolo[3,4-b]pyridine

(1-t-Butoxycarbonylindol-3-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.6 g) was added to trifluoroacetic acid (15 mL) under ice-cooling and the mixture was stirred for 3 hours. The solvent was evaporated under reduced pressure, 30 and ethyl acetate and a saturated aqueous sodium hydrogencarbonate solution were added to neutralize the mixture. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was

recrystallized from ethyl acetate to give the title compound (0.4 g) as colorless crystals.

MP:238°C.

Anal. Calcd. for: $C_{21}H_{13}N_7O \cdot 3/5 H_2O$: C, 64.64; H, 3.67; N, 25.13.

5 Found: C, 64.77; H, 4.05; N, 25.59.

MS (EI): 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.56 (1H, s), 7.08 (1H, dd, J=7.3Hz and 7.2Hz), 7.15 (1H, dd, J=7.3Hz and 7.2Hz), 7.44 (1H, s), 7.44-7.54 (3H, m), 7.65 (1H, dd, J=7.3Hz and 7.2Hz), 7.76 (1H, s),
10 7.95 (1H, d, J=7.3Hz), 9.98 (1H, brs), 11.63 (1H, brs), 12.20 (1H, brs).

Example 336

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-dimethoxymethyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
15 dimethylacetate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:212°C.

Anal. Calcd. for: $C_{19}H_{21}ClN_4O_2$: C, 61.21; H, 5.68; N, 15.03.

Found: C, 61.25; H, 5.69; N, 15.17.

20 MS (EI): 372 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88 (3H, t, J=7.3Hz), 1.57-1.63 (2H, m), 2.28-2.35 (2H, m), 2.93 (6H, s), 4.93 (1H, s), 5.30 (1H, s), 7.10 (1H, d, J=7.3Hz), 7.19 (1H, dd, J=7.3Hz and 7.2Hz), 7.25 (1H, dd, J=7.3Hz and 7.2Hz), 7.35 (1H, d, J=7.3Hz),
25 9.80 (1H, brs), 12.29 (1H, brs).

Example 337

5-Cyano-4,7-dihydro-6-propyl-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate,
30 pyridine-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:224°C.

Anal. Calcd. for: $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40.

Found: C, 67.90; H, 5.79; N, 26.31.

MS (EI): 265 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, $J=7.3\text{Hz}$), 1.62-1.67 (2H, m), 2.35-2.43 (2H, m), 4.95 (1H, s), 7.20 (2H, dd, $J=4.6\text{Hz}$ and 1.5Hz), 7.29 (1H, s), 8.50 (2H, dd, $J=4.6\text{Hz}$ and 1.5Hz), 9.84 (1H, brs), 12.20 (1H, brs).

Example 338

5-Cyano-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl butyrate, 3-methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 250°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{17}\text{N}_5\text{O}_2$: C, 63.15; H, 5.30; N, 21.66.

15 Found: C, 62.89; H, 5.51; N, 22.11.

MS (EI): 323 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, $J=7.3\text{Hz}$), 1.63-1.68 (2H, m), 2.26 (3H, s), 2.36-2.42 (2H, m), 4.83 (1H, s), 7.17 (1H, s), 7.20 (1H, d, $J=7.3\text{Hz}$), 7.32 (1H, d, $J=7.3\text{Hz}$), 7.48 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 9.91 (1H, brs), 12.22 (1H, brs).

Example 339

5-Cyano-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl isobutyrate, 3-methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 261°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{17}\text{N}_5\text{O}_2 \cdot 1/2 \text{H}_2\text{O}$: C, 61.43; H, 5.46; N, 21.07.

Found: C, 61.82; H, 5.32; N, 21.31.

30 MS (EI): 323 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.21 (3H, d, $J=7.2\text{Hz}$), 1.26 (3H, d, $J=7.2\text{Hz}$), 2.25 (3H, s), 3.01 (1H, t, $J=7.2\text{Hz}$), 4.84 (1H, s), 7.17 (1H, s), 7.22 (1H, d, $J=7.3\text{Hz}$), 7.32 (1H, d, $J=7.3\text{Hz}$),

7.48 (1H, dd, J=7.3Hz and 7.2Hz), 9.71 (1H, brs), 12.24 (1H, brs).

Example 340

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl cyclopropanecarboxylate, 3-methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 265°C.

Anal. Calcd. for: C₁₇H₁₅N₅O₂: C, 63.54; H, 4.71; N, 21.79.

10 Found: C, 63.44; H, 4.85; N, 22.04.

MS (EI): 321 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.90-1.07 (4H, m), 1.96-1.99 (1H, m), 2.26 (3H, s), 4.81 (1H, s), 7.17 (1H, s), 7.20 (1H, d, J=7.3Hz), 7.32 (1H, d, J=7.3Hz), 7.48 (1H, dd, J=7.3Hz and
15 7.2Hz), 9.23 (1H, brs), 12.23 (1H, brs).

Example 341

Ethyl 4-(2,1,3-benzoxazol-4-yl)-4,7-dihydro-6-(1-methylethyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 ethyl acetate

20 The title compound was prepared from 2,1,3-benzoxazole-4-aldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner as in Example 275.

MP: 190-193°C (decomposition)

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.7.3 (3H, t, J=7.1Hz), 1.19 (3H, d, J=7.1Hz), 1.29 (3H, d, J=7.1Hz), 3.77 (2H, m), 4.37 (1H, m),
25 5.69 (1H, s), 7.12 (1H, d, J=6.6Hz), 7.22 (1H, s), 7.51 (1H, dd, J=6.6, 9.0Hz), 7.78 (1H, d, J=8.8Hz), 9.31 (1H, brs), 12.02 (1H, brs).

Example 342

Ethyl 4-(2-nitrophenyl)-4,7-dihydro-6-(1-methylethyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate
30

 The title compound was prepared from 2-nitrobenzaldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner as in Example 275.

MP:205-206°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.78 (3H, t, J=6.8Hz),
1.15 (3H, d, J=7.1Hz), 1.26 (3H, d, J=7.1Hz), 3.71 (2H, m), 4.33 (1H, m),
5.44 (1H, s), 7.29-7.34 (3H, m), 7.58 (1H, m), 7.78 (1H, d, J=8.0Hz),
5 9.33 (1H, brs), 12.11 (1H, brs).

Example 343

Ethyl 4-(2-methoxyphenyl)-4,7-dihydro-6-(1-methylethyl)-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 ethyl acetate

The title compound was prepared from 2-
10 methoxybenzaldehyde, 3-aminopyrazole and ethyl
isobutyrylacetate in the same manner as in Example 275.
MP:179-180°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.81 (3H, t, J=7.1Hz),
1.17 (3H, d, J=7.1Hz), 1.27 (3H, d, J=7.1Hz), 3.76 (2H, m), 3.85 (3H, s),
15 4.31 (1H, m), 5.46 (1H, s), 6.77 (1H, m), 6.89 (1H, d, J=8.0Hz),
6.94 (1H, d, J=7.6Hz), 7.04 (1H, m), 7.14 (1H, s), 8.98 (1H, brs),
11.86 (1H, brs).

Example 344

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-cyclopropyl-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from
cyclopropanecarbonyl chloride, 2-bromobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 277.
MP:168-170°C

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86 (3H, t, J=7.1Hz), 0.87-
0.90 (2H, m), 1.10-1.14 (2H, m), 3.16 (1H, m), 3.78 (2H, m),
5.57 (1H, s), 7.01 (1H, dd, J=5.8, 7.6Hz), 7.09 (1H, d, J=7.8Hz),
7.24 (1H, m), 7.29 (1H, s), 7.51 (1H, d, J=6.8Hz), 8.65 (1H, brs),
12.01 (1H, brs).

30 **Example 345**

Ethyl 4-(2-bromo3-cyanophenyl)-4,7-dihydro-6-cyclopropyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from

cyclopropanecarbonyl chloride, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP:168-170°C

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=7.1Hz), 0.88-
5 1.00(2H, m), 1.10-1.18(2H, m), 3.14(1H, m), 3.80(2H, m),
5.64(1H, s), 7.33(1H, s), 7.34-7.49(2H, m), 7.68(1H, m),
8.77(1H, brs), 12.10(1H, brs).

Example 346

4-(2-Chlorophenyl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-
10 pyrazolo[3,4-b]pyridine

A solution of 3-aminopyrazole (3.0 g), di-t-butyl dicarbonate (17.3 g) and dimethylaminopyridine (1.3 g) in tetrahydrofuran (360 ml) was stirred at room temperature. The reaction mixture was concentrated under reduced pressure. The
15 obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a mixture (7.9 g) of 1-(t-butoxycarbonyl)-3-(t-butoxycarbonylamino)pyrazole and 2-(t-butoxycarbonyl)-3-(t-butoxycarbonylamino)pyrazole as a white amorphous solid. To a
20 suspension of the obtained white amorphous solid (7.9 g) and sodium hydride (1.1 g) in DMF (80 ml) was added methyl iodide (4.0 g) under ice-cooling and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added water under ice-cooling and the resulting mixture was
25 extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to
30 give a white solid (5.3 g). The obtained white solid (5.3 g) was dissolved in methylene chloride (50 ml), and trifluoroacetic acid (7 ml) was added. The resulting mixture was stirred at room temperature for 20 hours. The reaction

mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: chloroform-methanol (10:1)) to give 3-methylaminopyrazole (1.54 g) as a colorless transparent oil.

- 5 Subsequently, the title compound was prepared from methyl butyrate, 2-chlorobenzaldehyde and 3-methylaminopyrazole in the same manner as in Example 94.

MP:170-171°C

Anal. Calcd. for: $C_{17}H_{17}N_4Cl$: C, 65.28; H, 5.48; N, 17.91.

- 10 Found: C, 65.14; H, 5.52; N, 17.72.

MS (EI): 312 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00 (3H, t, $J=7.3$ Hz), 1.68 (2H, m), 2.62 (2H, m), 3.36 (3H, s), 5.36 (1H, s), 7.22-7.26 (2H, m), 7.30-7.32 (2H, m), 7.42 (1H, d, $J=8.1$ Hz), 12.31 (1H, brs).

15 **Example 347**

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

- The title compound was prepared from methyl butyrate, 2,1,3-benzoxazole-4-aldehyde and 3-methylaminopyrazole in the same manner as in Example 346.

MP:198-200°C

Anal. Calcd. for: $C_{17}H_{16}N_6O$: C, 63.74; H, 5.03; N, 26.23.

Found: C, 63.78; H, 5.12; N, 26.47.

MS (EI): 320 (M^+).

- 25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.97 (3H, t, $J=7.4$ Hz), 1.61 (2H, m), 2.63 (2H, m), 3.41 (3H, s), 5.40 (1H, s), 7.32 (1H, s), 7.40 (1H, d, $J=6.6$ Hz), 7.59 (1H, dd, $J=6.5, 6.6$ Hz), 7.92 (1H, d, $J=9.3$ Hz), 12.30 (1H, brs).

Example 348

- 30 4-(2-Bromo-3-cyanophenyl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 2-bromo-3-cyanobenzaldehyde and 3-methylaminopyrazole in the

same manner as in Example 346.

MP: 218-220°C

Anal. Calcd. for: C₁₈H₁₆N₅Br: C, 56.56; H, 4.22; N, 18.32.

Found: C, 56.60; H, 4.41; N, 18.18.

5 MS (EI): 382 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.00 (3H, t, J=7.3Hz), 1.63 (2H, m), 2.62 (2H, m), 3.37 (3H, s), 5.47 (1H, s), 7.39 (1H, s), 7.56-7.58 (2H, m), 7.83 (1H, m), 12.41 (1H, brs).

Example 349

10 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl acetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 2.14 (3H, s), 5.35 (1H, s), 7.21-7.33 (4H, m), 7.42 (1H, d, J=8.1Hz), 9.87 (1H, brs), 12.15 (1H, brs).

Example 350

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

20 A solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (22.9 g), di-t-butyl dicarbonate (19.4 g) and dimethylaminopyridine (0.5 g) in tetrahydrofuran (200 ml) was stirred at room temperature for 30 minutes. The reaction mixture was ice-cooled and the
25 precipitated crystals were collected by filtration to give 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (21.8 g) as white crystals. 2-(t-Butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (5.0 g), N-bromosuccinimide
30 (2.5 g) and azobisisobutyronitrile (66 mg) were suspended in benzene (50 ml) and the suspension was stirred for 1 hour. The reaction mixture was concentrated under reduced pressure, and the obtained residue was purified by silica gel column

chromatography (eluent: hexane-ethyl acetate (2:1)) and crystallized from ethyl acetate to give 6-bromomethyl-2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine as white crystals. To a suspension of
5 sodium hydride (32 mg) in DMF (10 ml) was added morpholine (70 μ l) and the mixture was stirred at room temperature for 30 minutes. To the reaction mixture was added 6-bromomethyl-2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.36 g) and the mixture was stirred
10 under ice-cooling for 1 hour. To the reaction mixture was added water, and the precipitated crystals were collected by filtration and washed with hexane to give 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine (450 mg) as
15 white crystals. A solution of 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine (440 mg) in trifluoroacetic acid (5 ml) was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure and
20 4M hydrochloric acid-dioxane solution was added. The precipitated crystals were collected by filtration and washed with ethyl acetate to give the title compound (250 mg) as pale-yellow crystals.

MP:210-214°C (decomposition).

25 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 3.20-3.40 (3H, m), 3.84-4.00 (3H, m), 4.17-4.40 (4H, m), 5.49 (1H, s), 7.26-7.37 (4H, s), 7.45 (1H, d, $J=7.8\text{Hz}$), 10.22 (1H, brs), 11.05 (1H, brs), 12.33 (1H, brs).

Example 351

30 6-Benzyloxymethyl-4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl benzyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in

the same manner as in Example 94.

MP: 165-166°C

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 4.35 (2H, d, J=2.9Hz), 4.57 (2H, s), 5.42 (1H, s), 7.24-7.45 (10H, m), 10.03 (1H, brs), 12.22 (1H, brs).

5 Example 352

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(methylpiperazin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

4-(2-Chlorophenyl)-5-cyano-6-(t-butyldimethylsilyloxy)-methyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine was prepared from ethyl t-butyldimethylsilyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94. To a solution of 4-(2-chlorophenyl)-5-cyano-6-(t-butyldimethylsilyloxy)methyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (10 g) in tetrahydrofuran (100 ml) was added a THF solution (24.9 ml) of 1.0 M tetrabutylammonium fluoride and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added ethyl acetate (200 ml), and the resulting mixture was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (5.46 g) as a white solid. To a solution of 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (1.0 g) and carbon tetrabromide (1.27 g) in methylene chloride (35 ml) was added triphenylphosphine (1.0 g) under ice-cooling and the mixture was stirred under ice-cooling for 4 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.45 g) as a pale-yellow solid. To a suspension of sodium hydride (25 mg)

in DMF (3 ml) was added 1-methylpiperazine (69 μ l) and the mixture was stirred at room temperature for 30 minutes. To this reaction mixture was added a solution of 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (200 mg) in DMF (3 ml) under ice-cooling and the mixture was stirred under ice-cooling for 1 hour. To the reaction mixture was added water and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: ethyl acetate-methanol (4:1)). The obtained oil was treated with hydrogen chloride-methanol to give the title compound (87 mg) as white crystals.

MP: 222-225°C (decomposition)

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.66-2.75(2H, m), 2.75(3H, s), 3.00-3.10(4H, m), 3.41-3.55(4H, m), 5.42(1H, s), 7.24-7.36(4H, m), 7.43(1H, d, $J=8.0\text{Hz}$), 9.77(1H, brs), 12.17(1H, brs).

Example 353

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(piperidin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine and piperidine in the same manner as in Example 352.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.43(1H, m), 1.67-1.82(5H, m), 3.05-3.25(2H, m), 3.48(2H, m), 4.10(2H, m), 5.49(1H, s), 7.26-7.35(4H, m), 7.45(1H, d, $J=8.0\text{Hz}$), 10.28(1H, brs), 10.59(1H, brs).

Example 354

Ethyl 4-(2-nitrophenyl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from cyclopropanecarbonyl chloride, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP:162-164°C (decomposition)

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.81 (3H, t, J=7.4Hz), 0.85-0.95 (2H, m), 1.10-1.18 (2H, m), 3.12 (1H, m), 3.72 (2H, m), 5.46 (1H, s), 7.27-7.34 (3H, m), 7.58 (1H, m), 7.78 (1H, d, J=8.0Hz),
5 8.78 (1H, brs), 12.12 (1H, brs).

Example 355

Ethyl 4-(2,1,3-benzoxazol-4-yl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from
10 cyclopropanecarbonyl chloride, 2,1,3-benzoxazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP:109-111°C (decomposition).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.76 (3H, t, J=6.8Hz), 0.85-0.86 (2H, m), 1.14-1.18 (2H, m), 3.12 (1H, m), 3.80 (2H, m),
15 5.69 (1H, s), 7.13 (1H, d, J=6.6Hz), 7.23 (1H, s), 7.51 (1H, m), 7.79 (1H, d, J=9.0Hz), 8.83 (1H, brs), 12.05 (1H, brs).

Example 356

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-4,7-dihydro-2-(phenylcarbamoyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was obtained as colorless crystals from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenylisocyanate in the same manner as in Example 204.

MS(EI):425 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91 (3H, t, J=7.3Hz), 1.64 (2H, m), 2.58 (2H, m), 5.44 (1H, s), 7.10 (1H, dd, J=6.3 and 7.6Hz), 7.31-7.34 (2H, m), 7.52 (1H, d, J=6.6Hz), 7.59-7.64 (3H, m), 7.95 (1H, s), 7.97 (1H, d, J=9.0Hz), 9.83 (1H, brs), 10.30 (1H, brs).

Example 357

30 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-1-(4-pentenoyl)-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine, dimethylaminopyridine and 4-pentenoyl chloride in the same manner as in Example 204.

MP:140°C.

Anal. Calcd. for: $C_{21}H_{21}ClN_4O$: C, 66.22; H, 5.62; N, 14.71.

5 Found: C, 66.20; H, 5.60; N, 14.65.

MS (EI) : 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, J=7.3Hz), 1.62 (2H, m),
2.39-2.58 (4H, m), 3.11 (2H, t, J=7.6Hz), 4.98 (1H, d, J=7.1Hz),
5.06 (1H, d, J=10.3Hz), 5.40 (1H, s), 5.85 (1H, m), 7.27-7.37 (4H, m),
10 7.46 (1H, d, J=7.0Hz), 9.58 (1H, brs).

Example 358

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2-(4-pentenoyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
15 from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and 4-pentenoyl chloride in the same manner as in Example 204.

MP:176-177°C.

Anal. Calcd. for: $C_{21}H_{21}ClN_4O$: C, 66.22; H, 5.56; N, 14.71.

20 Found: C, 66.15; H, 5.63; N, 14.55.

MS (EI) : 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, J=7.3Hz), 1.67 (2H, m),
2.34-2.49 (4H, m), 3.00 (2H, t, J=7.6Hz), 4.96 (1H, d, J=10.6Hz),
5.02 (1H, d, J=27.1Hz), 5.36 (1H, s), 5.82 (1H, m), 7.30-7.35 (3H, m),
25 7.46 (1H, d, J=7.8Hz), 7.83 (1H, s), 10.39 (1H, brs).

Example 359

5-Cyano-4,7-dihydro-4-(6-methylpyridin-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 6-
30 methylpyridine-2-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:177-181°C.

Anal. Calcd. for: $C_{16}H_{17}N_5 \cdot 4/5 H_2O$: C, 65.42; H, 6.38; N, 23.84.

Found: C, 65.52; H, 6.31; N, 24.19.

MS (EI): 279 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, $J=7.6\text{Hz}$), 1.66 (2H, m),
2.41 (2H, m), 2.43 (3H, s), 4.94 (1H, s), 6.98 (1H, d, $J=7.6\text{Hz}$),
5 7.06 (1H, d, $J=7.5\text{Hz}$), 7.21 (1H, s), 7.62 (1H, dd, $J=7.6$ and 7.7Hz),
9.71 (1H, brs), 12.09 (1H, brs).

Example 360

4-(5-Cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine)pyridine-N-oxide

10 The title compound was prepared from methyl butyrate, pyridine-4-aldehyde-N-oxide and 3-aminopyrazole in the same manner as in Example 94.

MP: 110-115°C.

Anal. Calcd. for: $\text{C}_{15}\text{H}_{15}\text{N}_5\text{O}$: C, 62.01; H, 6.18; N, 24.11.

15 Found: C, 61.94; H, 5.85; N, 23.73.

MS (EI): 283 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, $J=7.3\text{Hz}$), 1.62 (2H, m),
2.36 (2H, m), 4.98 (1H, s), 7.18 (2H, d, $J=6.6\text{Hz}$), 7.31 (1H, s),
8.14 (2H, d, $J=6.3\text{Hz}$), 9.86 (1H, brs), 12.2 (1H, brs).

20 Example 361

5-Cyano-4,7-dihydro-4-(3-(4-morpholinomethyl)phenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-(4-morpholinomethyl)benzaldehyde and 3-aminopyrazole in the
25 same manner as in Example 94.

MS (EI): 363 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, $J=7.3\text{Hz}$), 1.63 (2H, m),
2.30 (4H, m), 2.30 (2H, m), 3.40 (2H, s), 3.53 (4H, m), 4.86 (1H, s),
7.05 (1H, d, $J=7.8\text{Hz}$), 7.10 (1H, d, $J=7.6\text{Hz}$), 7.14 (1H, s), 7.19 (1H, s),
30 7.23 (1H, dd, $J=7.5$ and 7.6Hz), 9.70 (1H, brs), 12.10 (1H, brs).

Example 362

4-(3-Bromophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:202-205°C.

5 Anal. Calcd. for: $C_{16}H_{15}BrN_4$: C, 55.99; H, 4.41; N, 16.32.

Found: C, 55.82; H, 4.46; N, 17.03.

MS (EI): 343 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H, t, J=7.3Hz), 1.63 (2H, m),
2.37 (2H, m), 4.92 (1H, s), 7.18 (1H, d, J=7.9Hz), 7.25 (1H, s),
10 7.28 (1H, d, J=7.8Hz), 7.33 (1H, s), 7.39 (1H, d, J=8.3Hz),
9.80 (1H, brs), 12.18 (1H, brs).

Example 363

5-Cyano-4,7-dihydro-4-(4-fluoro-2-chlorophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl butyrate, 2-chloro-4-fluorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:209-212°C.

Anal. Calcd. for: $C_{16}H_{14}ClFN_4$: C, 60.67; H, 4.45; N, 17.69.

20 Found: C, 60.48; H, 4.48; N, 17.87.

MS (EI): 316 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H, t, J=7.3Hz), 1.64 (2H, m),
2.39 (2H, m), 5.33 (1H, s), 7.17-7.40 (3H, m), 7.41 (1H, dd, J=2.7 and
6.1Hz), 9.85 (1H, brs), 12.17 (1H, brs).

25 Example 364

5-Cyano-4,7-dihydro-4-(3-(morpholin-4-yl)phenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-(morpholin-4-yl)benzaldehyde and 3-aminopyrazole in the same
30 manner as in Example 94.

MP:196-200°C.

Anal. Calcd. for: $C_{20}H_{23}N_5O$: C, 68.47; H, 6.63; N, 20.04.

Found: C, 68.41; H, 6.77; N, 20.16.

MS (EI) : 349 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.92 (3H, t, J=7.3Hz), 1.63 (2H, m),
2.32 (2H, m), 3.05 (4H, t, J=4.6Hz), 7.71 (4H, t, J=4.6Hz), 4.80 (1H, s),
6.59 (1H, d, J=7.5Hz), 6.74 (1H, m), 6.76 (1H, s), 7.13 (1H, dd, J=7.8
5 and 7.8Hz), 7.21 (1H, s), 9.67 (1H, brs), 12.02 (1H, brs) .

Example 365

5-Cyano-4,7-dihydro-4-(3-(morpholin-4-yl)phenyl)-6-isopropyl- 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
10 3-(morpholin-4-yl)benzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 254-257°C.

Anal. Calcd. for: C₂₀H₂₃N₅O: C, 68.47; H, 6.63; N, 20.04.

Found: C, 68.56; H, 6.73; N, 20.30.

15 MS (EI) : 349 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.20 (3H, d, J=7.0Hz),
1.22 (3H, d, J=7.1Hz), 3.02 (2H, m), 3.04 (4H, t, J=4.8Hz),
3.70 (4H, t, J=4.8Hz), 4.78 (1H, s), 6.59 (1H, d, J=7.6Hz), 7.74 (1H, s),
7.13 (1H, dd, J=7.5 and 8.1Hz), 7.22 (1H, s), 9.48 (1H, brs),
20 12.09 (1H, brs) .

Example 366

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(3-(morpholin-4- yl)phenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
25 cyclopropanecarboxylate, 3-(morpholin-4-yl)benzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

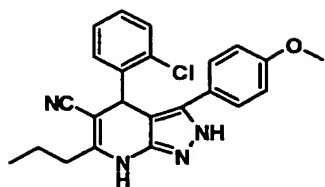
MP: >260°C.

MS (EI) : 347 (M⁺) .

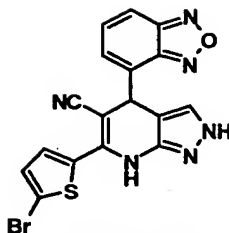
¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.86 (4H, m), 1.93-1.98 (1H, m),
30 3.05 (4H, t, J=4.6Hz), 3.70 (4H, t, J=4.6Hz), 4.79 (1H, s),
6.56 (1H, d, J=7.5Hz), 6.74 (1H, s), 6.77 (1H, s), 7.13 (1H, dd, J=7.8
and 7.8Hz), 7.20 (1H, s), 8.98 (1H, brs), 12.09 (1H, brs) .

The compounds of the above-described Examples are as

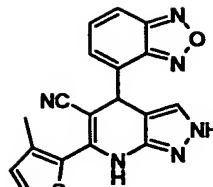
follows.



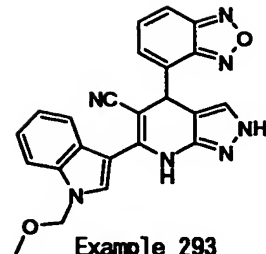
Example 290



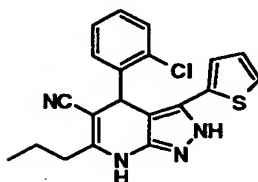
Example 291



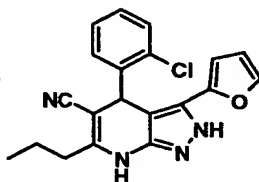
Example 292



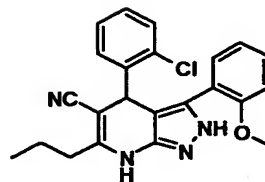
Example 293



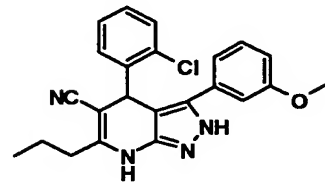
Example 294



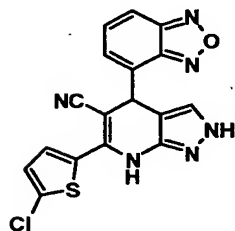
Example 295



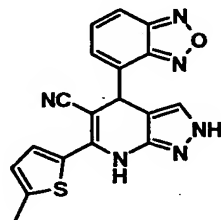
Example 296



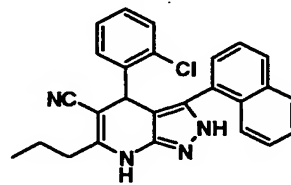
Example 297



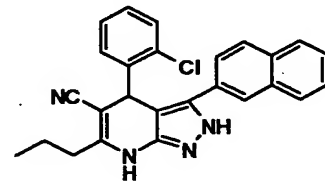
Example 298



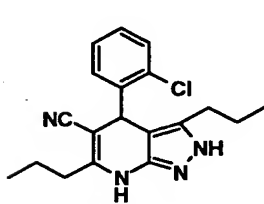
Example 299



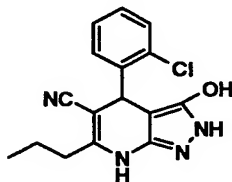
Example 300



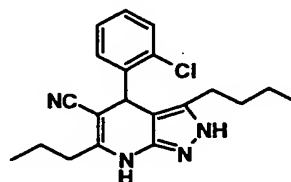
Example 301



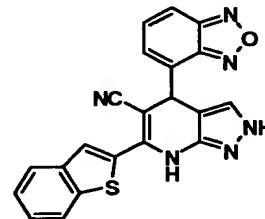
Example 302



Example 303



Example 304



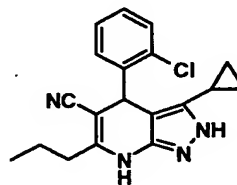
Example 305



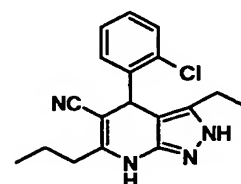
Example 306



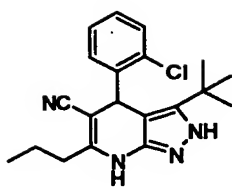
Example 307



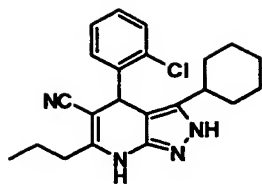
Example 308



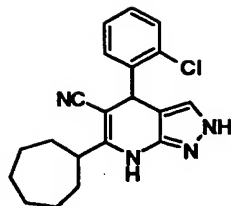
Example 309



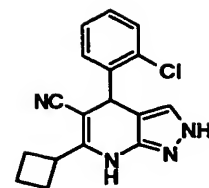
Example 310



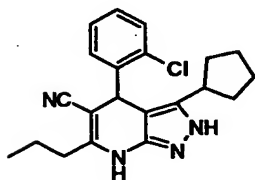
Example 311



Example 312



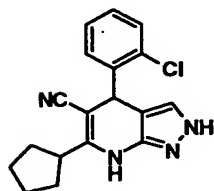
Example 313



Example 314



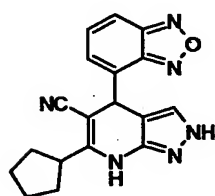
Example 315



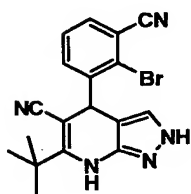
Example 316



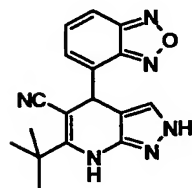
Example 317



Example 318



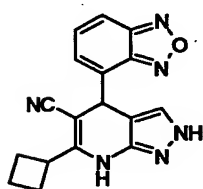
Example 319



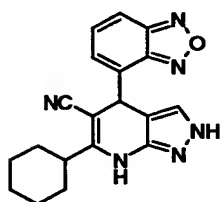
Example 320



Example 321



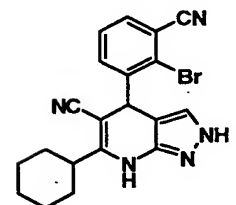
Example 322



Example 323



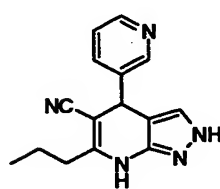
Example 324



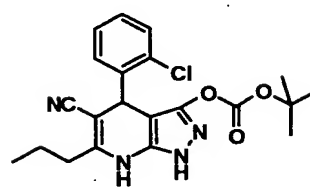
Example 325



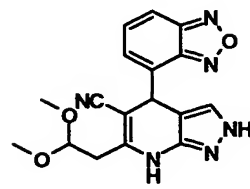
Example 326



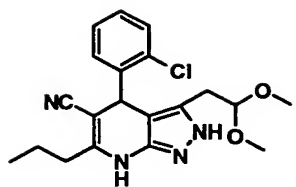
Example 327



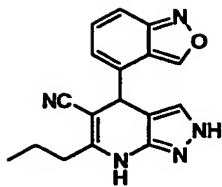
Example 328



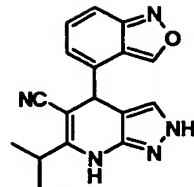
Example 329



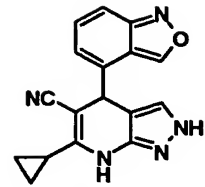
Example 330



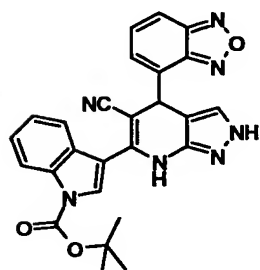
Example 331



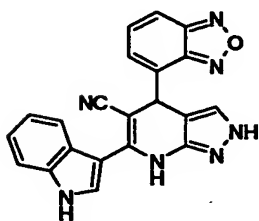
Example 332



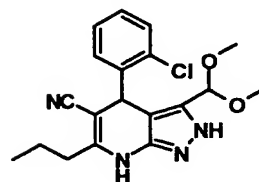
Example 333



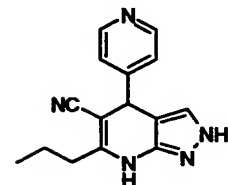
Example 334



Example 335



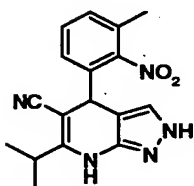
Example 336



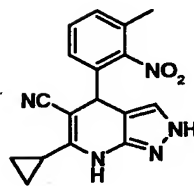
Example 337



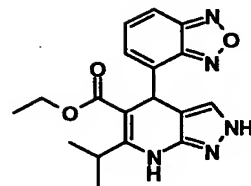
Example 338



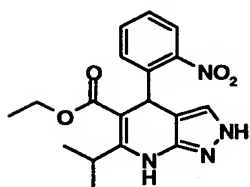
Example 339



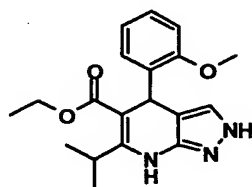
Example 340



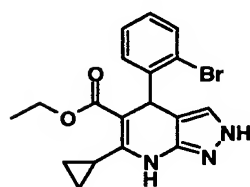
Example 341



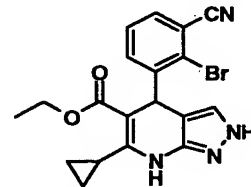
Example 342



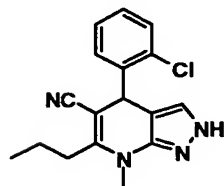
Example 343



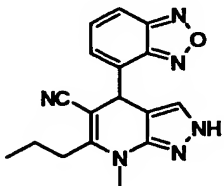
Example 344



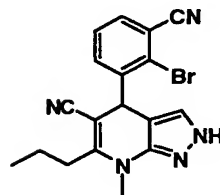
Example 345



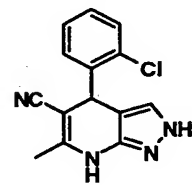
Example 346



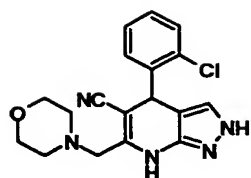
Example 347



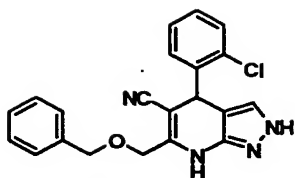
Example 348



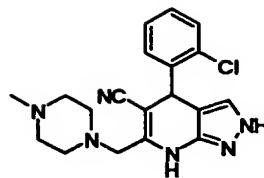
Example 349



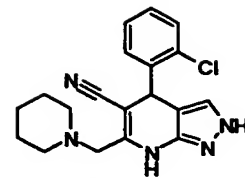
Example 350



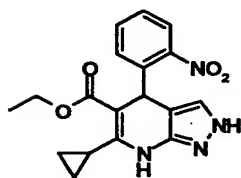
Example 351



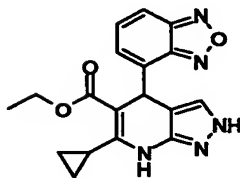
Example 352



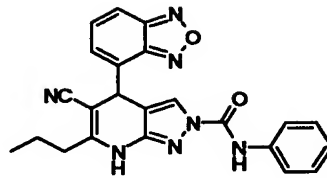
Example 353



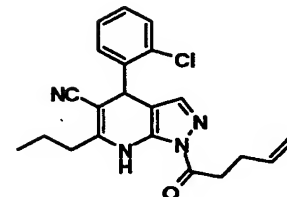
Example 354



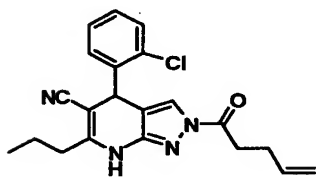
Example 355



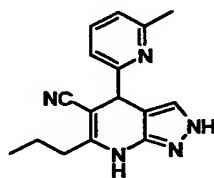
Example 356



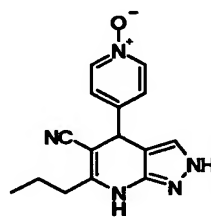
Example 357



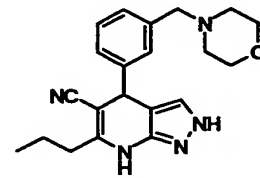
Example 358



Example 359



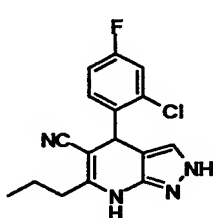
Example 360



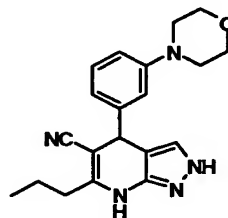
Example 361



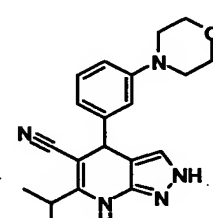
Example 362



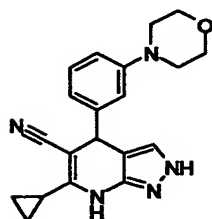
Example 363



Example 364



Example 365



Example 366

Example 1001

4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-*t*-butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-*b*]pyridine

To a solution of ethyl isonipecotate (10.0 g) in THF (200
5 mL) was added triethylamine (7.8 g), 4-dimethylaminopyridine
(0.8 g) and di-*tert*-butyldicarbonate (15.3 g) at 0°C and the
mixture was stirred for an hour. The mixture was extracted
with ethyl acetate and the solvent was evaporated under
reduced pressure to give ethyl *N*-Boc-piperidine-4-carboxylate
10 (16.3 g) as a colorless oil. To a solution of acetonitrile
(3.2 g) in THF (300 mL) was added *n*-BuLi (44 mmol) at -78°C and
stirred for three hours. Further, ethyl *N*-Boc-piperidine-4-
carboxylate (16.3 g) was added and the mixture was stirred for
an hour. After acidification with hydrochloric acid, the
15 mixture was extracted with ethyl acetate. The solvent was
evaporated under reduced pressure and the residue was purified
by silica gel column chromatography (eluent: hexane-ethyl
acetate (5:1)) to give 1-(*N*-Boc-piperidin-4-yl)-2-cyanoethan-
1-one (11.6 g) as a colorless oil. A solution of 2,1,3-
20 benzoxadiazole-4-aldehyde (1.0 g), 3-aminopyrazole (0.6 g) and
2-(*N*-Boc-piperidin-4-yl)-1-cyanoethan-2-one (1.7 g) in
acetonitrile (10 mL) was heated under reflux overnight. The
reaction mixture was cooled to room temperature, and the
precipitated crystals were collected by filtration to give the
25 title compound (2.0 g) as colorless crystals.

MP: 226°C.

Anal. Calcd. For: C₂₃H₂₅N₇O₃: C, 61.73; H, 5.63; N, 21.97.

Found: C, 61.45; H, 5.82; N, 21.61.

MS (EI): 447 (M⁺).

30 ¹H-NMR (400 MHz, DMSO-*d*₆) δ (ppm): 1.42 (9H, m), 1.59-1.62 (2H, m),
1.89-1.92 (2H, m), 2.62-2.86 (3H, m), 4.05-4.08 (2H, m), 5.40 (1H, s),
7.26 (1H, s), 7.41 (1H, d, J=6.6 Hz), 7.58 (1H, dd, J=9.0 Hz and 6.6 Hz),
7.92 (1H, d, J=9.0 Hz), 9.81 (1H, brs), 12.24 (1H, brs).

Example 1002

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-t-butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (1.7 g) was added to trifluoroacetic acid (20 mL) at 0°C and the mixture was stirred for an hour. The solvent was evaporated under reduced pressure. After alkalification with sodium bicarbonate, the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was washed with acetonitrile, and the precipitated crystals were collected by filtration to give the title compound (0.83 g) as yellow crystals.

MP:216°C.

MS (EI) : 348 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.78-1.81 (2H, m), 2.07-2.11 (2H, m), 2.80-2.86 (3H, m), 3.27-3.30 (3H, m), 5.39 (1H, s), 7.27 (1H, s), 7.43 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz), 9.86 (1H, brs), 12.24 (1H, brs).

Example 1003

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine (0.7 g) in MeOH (200 mL) was added 37% formaldehyde (0.18 g), sodium cyanoborohydride (0.19 g) and acetic acid (0.36 g) at room temperature and the mixture was stirred overnight. After alkalification with sodium bicarbonate, the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was washed with acetonitrile, and the precipitated crystals were collected by filtration to give the title compound (0.32 g) as yellow crystals.

MP:>270°C.

MS (EI) : 361 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.57-1.60 (2H, m) , 1.82-1.88 (2H, m) ,
2.01-2.06 (2H, m) , 2.15 (3H, s) , 2.58-2.61 (1H, m) , 2.85-2.88 (2H, m) ,
5.40 (1H, s) , 7.26 (1H, s) , 7.40 (1H, d, J=6.6Hz) , 7.58 (1H, dd, J=9.0Hz
5 and 6.6Hz) , 7.91 (1H, d, J=9.0Hz) , 9.76 (1H, brs) , 12.17 (1H, brs) .

Example 1004

4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-t-butoxycarbonylpiperidin-3-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl nipecotate,
10 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 1001.

MP: 229°C.

Anal. Calcd. For: C₂₃H₂₅N₇O₃: C, 61.73; H, 5.63; N, 21.97.

Found: C, 61.56; H, 5.66; N, 21.67.

15 MS (EI) : 447 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.32-1.40 (2H, m) , 1.39 (9H, s) ,
1.69-1.78 (2H, m) , 2.69-2.76 (2H, m) , 3.16-3.19 (1H, m) , 3.92-
3.95 (2H, m) , 5.42 (1H, s) , 7.28 (1H, s) , 7.42 (1H, d, J=6.6Hz) ,
7.58 (1H, dd, J=9.0Hz and 6.6Hz) , 7.92 (1H, d, J=9.0Hz) ,
20 9.87 (1H, brs) , 12.21 (1H, brs) .

Example 1005

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-
25 4-yl)-6-(1-t-butoxycarbonylpiperidin-3-yl)-5-cyano-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in
Example 1002.

MP: 202°C.

Anal. Calcd. For: C₁₈H₁₇N₇O: C, 62.24; H, 4.93; N, 28.23.

30 Found: C, 61.97; H, 5.13; N, 27.89.

MS (EI) : 347 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.42-1.45 (1H, m) , 1.72-1.88 (3H, m) ,
2.66-2.84 (5H, m) , 2.94-3.02 (1H, m) , 5.38 (1H, s) , 7.26 (1H, s) ,

7.39 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and 6.6Hz),
7.91 (1H, d, J=9.0Hz), 10.39 (1H, brs), 12.17 (1H, brs).

Example 1006

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-
5 methylpiperidin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-3-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.

MP:228°C.

10 MS (EI): 361 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.53-1.76 (4H, m), 2.21 (3H, s),
2.47-2.55 (4H, m), 2.93-2.96 (1H, m), 5.38 (1H, s), 7.27 (1H, s),
7.40 (1H, d, J=6.6Hz), 7.59 (1H, dd, J=9.0Hz and 6.6Hz),
7.92 (1H, d, J=9.0Hz), 10.16 (1H, brs), 12.20 (1H, brs).

15 **Example 1007**

4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-t-butoxycarbonylpiperidin-2-
yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl pipecolate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
20 same manner as in Example 1001.

MS (EI): 447 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.27 and 1.32 (9H, s), 1.42-
1.97 (6H, m), 3.30-3.33 (1H, m), 3.53-3.61 (1H, m), 4.47-4.50 (1H, m),
5.37 and 5.39 (1H, s), 7.26 and 7.29 (1H, s), 7.38-7.44 (1H, m),
25 7.54-7.60 (1H, m), 7.90-7.93 (1H, m), 9.63 and 9.73 (1H, brs),
12.16 (1H, brs).

Example 1008

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-
2-yl)-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-6-(1-t-butoxycarbonylpiperidin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

MS (EI) : 347 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.27-1.88 (6H, m), 3.12-3.16 (1H, m),
4.12-4.15 (1H, m), 4.48-4.58 (1H, m), 5.64 and 5.66 (1H, s), 7.22-
7.28 (1H, m), 7.45-7.52 (2H, m), 7.87-7.90 (1H, m), 8.26 (1H, br),
5 10.92 and 10.94 (1H, brs), 12.35 (1H, brs) .

Example 1009

4-(2,1,3-Benzoxadiazol-4-yl)-6-(4-t-butoxycarbonylmorpholin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl morpholine-2-
10 carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-amino-
pyrazole in the same manner as in Example 1001.

MS (EI) : 449 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.36 and 1.40 (9H, s), 2.95-
3.06 (2H, m), 3.50-3.52 (1H, m), 3.75-3.95 (3H, m), 4.34-4.40 (1H, m),
15 5.44 and 5.48 (1H, s), 7.26 and 7.30 (1H, s), 7.42-7.45 (1H, m),
7.57-7.62 (1H, m), 7.93-7.96 (1H, m), 9.84 and 9.92 (1H, brs),
12.23 (1H, brs) .

Example 1010

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(morpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-
diazol-4-yl)-6-(4-t-butoxycarbonylmorpholin-2-yl)-5-cyano-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in
Example 1002.

25 MS (EI) : 349 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 2.64-2.95 (4H, m), 3.53 (1H, br),
3.55-3.57 (1H, m), 3.82-3.85 (1H, m), 4.41-4.45 (1H, m), 5.43 and
5.44 (1H, s), 7.24 and 7.28 (1H, s), 7.38-7.41 (1H, m), 7.56-
7.61 (1H, m), 7.91-7.94 (1H, m), 9.74 and 9.76 (1H, brs),
30 12.19 (1H, brs) .

Example 1011

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methylmorpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-diazol-4-yl)-5-cyano-4,7-dihydro-6-(morpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.
MP:143°C.

5 MS(EI):363(M⁺).

¹H-NMR(400MHz,DMSO-d₆)δ(ppm): 2.21(3H,s), 2.19-2.30(2H,m),
2.60-2.69(2H,m), 3.60-3.62(1H,m), 3.88-3.92(1H,m), 4.48-
4.50(1H,m), 5.44(1H,s), 7.28(1H,s), 7.39(1H,d,J=6.6Hz),
7.58(1H,dd,J=9.0Hz and 6.6Hz), 7.92(1H,d,J=9.0Hz),
10 9.80(1H,brs), 12.20(1H,brs).

Example 1012

4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-t-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from ethyl 1,2,3,6-tetrahydropyridine-4-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MP:222°C.

20 MS(EI):445(M⁺).

¹H-NMR(400MHz,DMSO-d₆)δ(ppm): 1.41(9H,s), 2.35-2.39(2H,m),
3.46-3.48(2H,m), 3.90-3.92(2H,m), 5.43(1H,s), 6.06-6.09(1H,m),
7.28(1H,s), 7.45(1H,d,J=6.6Hz), 7.60(1H,dd,J=9.0Hz and 6.6Hz),
7.93(1H,d,J=9.0Hz), 9.94(1H,brs), 12.19(1H,brs).

25 Example 1013

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-diazol-4-yl)-6-(1-t-butoxycarbonyl-1,2,3,6-tetrahydropyridin-
30 4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

MP:180°C.

MS(EI):345(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 2.26-2.32 (2H, m), 2.87-2.90 (2H, m), 3.30-3.36 (3H, m), 5.42 (1H, s), 6.09-6.10 (1H, m), 7.30 (1H, s), 7.43 (1H, d, J=6.6Hz), 7.60 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz), 9.87 (1H, brs), 12.18 (1H, brs).

5 **Example 1014**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.

MP: 218°C.

MS (EI): 359 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 2.24 (3H, s), 2.35-2.42 (2H, m), 2.91-2.93 (2H, m), 3.31-3.33 (2H, m), 5.42 (1H, s), 6.04-6.05 (1H, m), 7.27 (1H, s), 7.43 (1H, d, J=6.6Hz), 7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz), 9.87 (1H, brs), 12.17 (1H, brs).

Example 1015

4-(2,1,3-Benzoxadiazol-4-yl)-6-(2-(N-t-butoxycarbonyl-N-methylamino)ethyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

To a solution of ethyl 3-aminopropionate hydrochloride (19 g) in THF (600 mL) was added triethylamine (44 mL), dimethylaminopyridine (1.5 g) and di-tert-butylidicarbonate (30 g) at 0°C and the mixture was stirred at 40°C for four hours. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure to give ethyl N-Boc-3-aminopropionate (16.7 g) as a colorless oil. To a solution of ethyl N-Boc-3-aminopropionate (5.0 g) in THF (50 mL) was added t-BuOK (2.8 g) and methyl iodide (4.9 g) at 0°C and the mixture was stirred at room temperature for an hour. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure to give ethyl 3-(N-Boc-N-

methylamino)propionate (4.3 g) as a colorless oil.

Subsequently, the title compound was prepared from ethyl 3-(N-Boc-N-methylamino)propionate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1001.

5 MP:240°C.

Anal. Calcd. For: C₂₁H₂₃N₇O₃: C, 59.85; H, 5.50; N, 23.26.

Found: C, 59.69; H, 5.45; N, 23.22.

MS (EI): 421 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.26 and 2.32 (9H, s), 2.62-
10 2.63 (2H, m), 2.81 (3H, s), 3.48-3.55 (2H, m), 5.40 (1H, s), 7.27
(1H, s), 7.40 (1H, d, J=6.6Hz), 7.57 (1H, dd, J=9.0Hz and 6.6Hz),
7.92 (1H, d, J=9.0Hz), 10.07 (1H, brs), 12.15 (1H, brs).

Example 1016

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-(N-
15 methylamino)ethyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-
diazol-4-yl)-6-(2-(N-t-butoxycarbonyl-N-methylamino)ethyl)-5-
cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same
manner as in Example 1002.

20 MP:174°C.

MS (EI): 321 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 2.29 (3H, s), 2.50-2.78 (4H, m),
3.31 (3H, br), 5.39 (1H, s), 7.24 (1H, s), 7.43 (1H, d, J=6.6Hz),
7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.91 (1H, d, J=9.0Hz).

25 Example 1017

4-(2,1,3-Benzoxadiazol-4-yl)-6-(2-(N-t-butoxycarbonyl-
amino)ethyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 3-aminopropionate
hydrochloride, 2,1,3-benzoxadiazole-4-aldehyde and 3-
30 aminopyrazole in the same manner as in Example 1001.

MP:231°C.

Anal. Calcd. For: C₂₀H₂₁N₇O₃: C, 58.96; H, 5.20; N, 24.06.

Found: C, 58.81; H, 5.19; N, 23.82.

MS (EI) : 407 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.33 (9H, s) , 2.55-2.60 (2H, m) ,
3.23-3.33 (2H, m) , 5.41 (1H, s) , 6.81 (1H, brs) , 7.25 (1H, s) ,
7.44 (1H, d, J=6.6Hz) , 7.57 (1H, dd, J=9.0Hz and 6.6Hz) ,
5 7.92 (1H, d, J=9.0Hz) , 9.94 (1H, brs) , 12.14 (1H, brs) .

Example 1018

6-(2-Aminoethyl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-
10 diazol-4-yl)-6-(2-(N-t-butoxycarbonylamino)ethyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

MS (EI) : 307 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 2.50-2.54 (2H, m) , 2.88
15 (2H, t, J=7.3Hz) , 3.35 (4H, br) , 5.40 (1H, s) , 7.25 (1H, s) ,
7.44 (1H, d, J=6.6Hz) , 7.58 (1H, dd, J=9.0Hz and 6.6Hz) ,
7.92 (1H, d, J=9.0Hz) .

Example 1019

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-(N,N-dimethylamino)ethyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-
diazol-4-yl)-5-cyano-4,7-dihydro-6-(2-(N-methylamino)ethyl)-
2H-pyrazolo[3,4-b]pyridine in the same manner as in Example
1003.

25 MP: 215°C.

MS (EI) : 335 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 2.19 (6H, s) , 2.45-2.62 (4H, m) ,
5.41 (1H, s) , 7.27 (1H, s) , 7.43 (1H, d, J=6.6Hz) , 7.58 (1H, dd, J=9.0Hz
and 6.6Hz) , 7.92 (1H, d, J=9.0Hz) , 10.04 (1H, brs) , 12.16 (1H, brs) .

30 **Example 1020**

4-(2,1,3-Benzoxadiazol-4-yl)-6-((N-t-butoxycarbonyl-N-methylamino)methyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from glycine ethyl ester hydrochloride, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1015.

MP:207°C.

5 Anal. Calcd. For: C₂₀H₂₁N₇O₃: C, 58.96; H, 5.20; N, 24.06.

Found: C, 58.80; H, 5.12; N, 24.38.

MS (EI): 407 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.33 and 1.39 (9H, s), 2.81 (3H, s),
4.13-4.20 (2H, m), 5.42 (1H, s), 7.29 (1H, s), 7.43 (1H, d, J=6.6Hz),
10 7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.94 (1H, d, J=9.0Hz),
9.33 (1H, brs), 12.15 (1H, brs).

Example 1021

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-((N-methylamino)methyl)-2H-pyrazolo[3,4-b]pyridine

15 trifluoroacetate

4-(2,1,3-Benzoxadiazol-4-yl)-6-((N-t-butoxycarbonyl-N-methylamino)methyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]-
pyridine (0.6 g) was added to trifluoroacetic acid (10 mL) at
0°C and the mixture was stirred for an hour. The solvent was
20 evaporated under reduced pressure and the residue was
crystallized by ethanol, and the precipitated crystals were
collected by filtration to give the title compound (0.1 g) as
yellow crystals.

MP:174°C.

25 MS (EI): 307 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 3.10 (3H, s), 4.51-4.68 (2H, m),
7.24 (1H, d, J=6.6Hz), 7.45 (1H, s), 7.52 (1H, dd, J=9.0Hz and 6.6Hz),
7.89 (1H, d, J=9.0Hz), 8.08-8.20 (2H, br), 10.81 (1H, brs),
12.41 (1H, brs).

30 **Example 1022**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-(N-methylamino)cyclohexyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 4-aminocyclo-

hexanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1015, and Example 1002 followed.

MS(EI): 375(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.32-1.35(2H,m), 1.81-2.12 (6H,m), 2.57(3H,s), 2.65-2.69(1H,m), 2.81-2.85(1H,m), 5.39 (1H,s), 7.28(1H,s), 7.41(1H,d,J=6.6Hz), 7.59(1H,dd,J=9.0Hz and 6.6Hz), 7.92(1H,d,J=9.0Hz), 8.54(1H,br), 9.79(1H,brs), 12.22(1H,brs).

Example 1023

10 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-(N,N-dimethylamino)cyclohexyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-(N-methylamino)-cyclohexyl)-2H-pyrazolo[3,4-b]pyridine in the same manner as
15 in Example 1003.

MP: 241°C.

MS(EI): 389(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.15-2.02(9H,m), 2.15 and 2.21(6H,s), 2.62-2.76(1H,m), 5.38 and 5.43(1H,s), 7.26(1H,s),
20 7.38-7.44(1H,m), 7.56-7.62(1H,m), 7.90-7.96(1H,m), 9.74(1H,brs), 12.18(1H,brs).

Example 1024

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-phenylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

25 To a solution of ethyl isonipecotatate (8.9 g) in CH₂Cl₂ (500 mL) was added triphenyl bismus (25 g) and Copper(II)acetate (10.3 g) at room temperature, the mixture was stirred overnight. After filtration, the mixture was extracted with CH₂Cl₂. The solvent was evaporated under reduced pressure and
30 the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give ethyl 1-phenylpiperidine-4-carboxylate (8.6 g) as colorless crystals. To a solution of acetonitrile (1.9 g) in THF (200 mL) was

added *n*-BuLi (41 mmol) at -78°C. Further, ethyl 1-phenylpiperidine-4-carboxylate (8.6 g) was added and the mixture was stirred for an hour. After acidification with hydrochloric acid, the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-(1-phenylpiperidin-4-yl)-2-cyanoethan-1-one (2.0 g) as colorless crystals. A solution of 2,1,3-benzoxadiazole-4-aldehyde (0.3 g), 3-aminopyrazole (0.2 g) and 1-(1-phenylpiperidin-4-yl)-2-cyanoethan-1-one (0.5 g) in acetonitrile (10 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (0.6 g) as colorless crystals.

MS (FAB) : 424 ($M^+ + 1$).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 1.73-1.76 (2H, m), 2.14-2.18 (2H, m), 2.62-2.66 (2H, m), 2.81-2.84 (1H, m), 3.80-3.84 (2H, m), 5.41 (1H, s), 6.75 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 6.94-6.96 (2H, m), 7.18-7.27 (3H, m), 7.42 (1H, d, $J=6.6\text{Hz}$), 7.59 (1H, dd, $J=9.0\text{Hz}$ and 6.6Hz), 7.92 (1H, d, $J=9.0\text{Hz}$), 9.81 (1H, brs), 12.17 (1H, brs).

Example 1025

6-(1-Acetylpiperidin-4-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-*b*]pyridine

To a solution of ethyl isonipecotate (8.0 g) in THF (100 mL) was added triethylamine (5.7 g), dimethylaminopyridine (0.6 g) and acetyl chloride (4.4 g) at 0°C and the mixture was stirred for an hour. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure to give ethyl 1-acetylpiperidine-4-carboxylate (10 g) as a colorless oil. To a solution of acetonitrile (2.5 g) in THF (300 mL) was added *n*-BuLi (57 mmol) at -78°C. Further, ethyl 1-acetylpiperidine-4-carboxylate (10 g) was added and the

mixture was stirred for an hour. After acidification with hydrochloric acid, the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-(1-acetylpiperidin-4-yl)-2-cyanoethan-1-one (7.5 g) as a colorless oil. A solution of 2,1,3-benzoxadiazole-4-aldehyde (0.3 g), 3-aminopyrazole (0.17 g) and 1-(1-acetylpiperidin-4-yl)-2-cyanoethan-1-one (0.4 g) in acetonitrile (10 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (0.49 g) as yellow crystals.

MP:248°C.

MS (FAB) : 340 ($M^+ + 1$).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.62-1.64 (2H, m), 1.82-1.84 (1H, m), 2.00-2.02 (4H, m), 2.49-2.50 (1H, m), 2.94-3.07 (2H, m), 3.89-3.92 (1H, m), 4.48-4.51 (1H, m), 5.40 (1H, s), 7.27 (1H, s), 7.42 (1H, d, $J=6.6\text{Hz}$), 7.59 (1H, dd, $J=9.0\text{Hz}$ and 6.6Hz), 7.92 (1H, d, $J=9.0\text{Hz}$), 9.81 (1H, brs), 12.18 (1H, brs).

Example 1026

4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-benzoylpiperidin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from benzoylchloride, ethyl isonipecotate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MP:228°C.

MS (FAB) : 452 ($M^+ + 1$).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.59-1.76 (2H, m), 2.04-2.08 (2H, m), 2.76-2.80 (1H, m), 3.01-3.09 (2H, m), 3.58-3.60 (1H, m), 4.60-4.63 (1H, m), 5.41 (1H, s), 7.28 (1H, s), 7.43-7.46 (6H, m), 7.56-7.59 (1H, m), 7.92 (1H, d, $J=9.0\text{Hz}$), 9.90 (1H, brs), 12.21 (1H, brs).

Example 1027

6-(1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]-pyridine

- 5 The title compound was prepared from acetyl chloride, ethyl 1,2,3,6-tetrahydropyridine-4-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MP:237°C.

- 10 MS (EI) : 387 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 2.00 and 2.04 (3H, s), 2.46-2.49 (2H, m), 3.55-3.58 (2H, m), 4.00-4.06 (2H, m), 5.44 (1H, s), 6.10 (1H, s), 7.29 (1H, s), 7.45 (1H, d, J=6.6Hz), 7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.93 (1H, d, J=9.0Hz), 9.94 (1H, brs), 12.17 (1H, brs) .

- 15 **Example 1028**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-(ethoxycarbonyl)piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

- The title compound was prepared from ethyl chloroformate, ethyl isonipecotate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MS (EI) : 419 (M⁺) .

- ¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.19 (3H, t, J=7.3Hz), 1.61-1.63 (2H, m), 1.90-1.94 (2H, m), 2.84-2.88 (3H, m), 4.02-4.07 (4H, m), 5.40 (1H, s), 7.26 (1H, s), 7.41 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz), 9.80 (1H, brs), 12.17 (1H, brs) .

Example 1029

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methanesulfonylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

- The title compound was prepared from methanesulfonyl-chloride, ethyl isonipecotate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MP:243°C.

MS (EI) : 425 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.73-1.76 (2H, m), 2.04-2.08 (2H, m), 2.74-2.78 (3H, m), 2.88 (3H, s), 3.66-3.69 (2H, m), 5.41 (1H, s), 7.27 (1H, s), 7.42 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.93 (1H, d, J=9.0Hz), 9.84 (1H, brs), 12.20 (1H, brs).

5 **Example 1030**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-(N,N--dimethylaminocarbonyl)piperidin-4-yl)-2H-pyrazolo[3,4-b]-pyridine

The title compound was prepared from 1-chloro-N,N-
10 dimethylformamide, ethyl isonipecotate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MS (EI): 418 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.61-1.63 (2H, m), 2.00-2.06 (2H, m),
15 2.65-2.67 (2H, m), 2.75 (6H, s), 2.81-2.85 (1H, m), 3.64-3.67 (2H, m), 5.40 (1H, s), 7.27 (1H, s), 7.41 (1H, d, J=6.6Hz), 7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz), 9.86 (1H, brs), 12.18 (1H, brs).

Example 1031

20 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-guanylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine (1.5 g) in MeOH (30 mL) was added diisopropylethylamine (4.2 g), and
25 1H-pyrazole-1-carboxamide hydrochloride (0.96 g) at room temperature and the mixture was stirred overnight. The precipitated crystals were collected by filtration to give the title compound (1.0 g) as yellow crystals.

MP: >270°C.

30 MS (EI): 389 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.53-1.56 (2H, m), 1.86-1.91 (2H, m), 2.47-2.50 (2H, m), 2.71-2.77 (1H, m), 3.00-3.03 (2H, m), 3.32-3.36 (3H, br), 5.39 (1H, s), 7.26 (1H, s), 7.39 (1H, d, J=6.6Hz),

7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.91 (1H, d, J=9.0Hz),
9.79 (1H, brs), 12.21 (1H, brs).

Example 1032

6-(1-Acetylpiperidin-3-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-
5 cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from acetyl chloride, ethyl nipecotate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MP:219°C.

10 Anal. Calcd. For: C₂₀H₁₉N₇O₂: C, 61.69; H, 4.92; N, 25.18.

Found: C, 61.36; H, 4.90; N, 25.12.

MS (EI): 389 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.25-1.49 (1H, m), 1.74-1.78 (2H, m),
2.00 (3H, s), 2.01-2.04 (1H, m), 2.49-2.98 (3H, m), 3.78-3.81 (1H, m),
15 4.37-4.40 (1H, m), 5.29 and 5.42 (1H, s), 7.28 (1H, s), 7.41-
7.48 (1H, m), 7.58-7.62 (1H, m), 7.92-7.95 (1H, m), 9.90 (1H, brs),
12.21 (1H, brs).

Example 1033

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-
20 ethylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine and acetaldehyde in the same manner as in Example 1003.

25 MP:231°C.

MS (EI): 375 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.99 (3H, t, J=7.3Hz), 1.60-
1.63 (2H, m), 1.85-1.88 (2H, m), 2.00-2.04 (2H, m), 2.31-2.34 (2H, m),
2.64-2.66 (1H, m), 2.97-3.00 (2H, m), 5.39 (1H, s), 7.26 (1H, s),
30 7.40 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and 6.6Hz),
7.92 (1H, d, J=9.0Hz), 9.75 (1H, brs), 12.18 (1H, brs).

Example 1034

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-

propylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-Benzoxa-
diazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-
pyrazolo[3,4-b]pyridine and propionaldehyde in the same manner
5 as in Example 1003.

MP:246°C.

Anal. Calcd. For: C₂₁H₂₃N₇O: C, 64.76; H, 5.95; N, 25.18.

Found: C, 64.23; H, 5.87; N, 24.86.

MS (EI) : 389 (M⁺).

10 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 0.84 (3H, t, J=7.3Hz), 1.40-1.45
(2H, m), 1.59-1.62 (2H, m), 1.82-1.86 (2H, m), 2.00-2.05 (2H, m),
2.21 (2H, t, J=7.3Hz), 2.62-2.65 (1H, m), 2.94-2.97 (2H, m), 5.39
(1H, s), 7.26 (1H, s), 7.40 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and
6.6Hz), 7.91 (1H, d, J=9.0Hz), 9.77 (1H, brs), 12.18 (1H, brs).

15 **Example 1035**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-iso-
propylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxa-
diazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-
20 pyrazolo[3,4-b]pyridine and acetone in the same manner as in
Example 1003.

MP:260°C.

MS (EI) : 389 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.22 (6H, d, J=7.3Hz), 1.82-3.42
25 (10H, m), 5.40 (1H, s), 7.27 (1H, s), 7.42 (1H, d, J=6.6Hz),
7.59 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz),
9.66 (1H, brs), 12.22 (1H, brs).

Example 1036

4-(2-Bromo-3-cyanophenyl)-6-(1-t-butoxycarbonylpiperidin-4-
30 yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl isonipecotate, 2-
bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 1001.

MP:>270°C.

Anal. Calcd. For: C₂₄H₂₅BrN₆O₂: C, 56.59; H, 4.95; N, 16.50.

Found: C, 56.47; H, 4.87; N, 16.52.

MS (EI): 509 (M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.41 (9H, s), 1.59-1.66 (2H, m),
1.85-1.90 (2H, m), 2.65-2.82 (3H, m), 4.05-4.07 (2H, m), 5.47 (1H, s),
7.33 (1H, s), 7.56-7.60 (2H, m), 7.84 (1H, d, J=7.3Hz), 9.81 (1H, brs),
12.26 (1H, brs).

Example 1037

10 4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromo-3-cyano-phenyl)-6-(1-t-butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in

15 Example 1002.

MP:>270°C.

MS (EI): 409 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.53-1.56 (2H, m), 1.83-1.87 (2H, m),
2.46-2.50 (3H, m), 2.71-2.74 (1H, m), 3.00-3.04 (1H, m), 5.45 (1H, s),
20 7.32 (1H, s), 7.56-7.58 (2H, m), 7.81 (1H, d, J=7.3Hz), 9.74 (1H, brs),
12.26 (1H, brs).

Example 1038

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from 4-(2-bromo-3-cyano-phenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo-[3,4-b]pyridine in the same manner as in Example 1003.

MP:>270°C.

MS (EI): 423 (M⁺).

30 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.65-1.71 (2H, m), 2.02-2.08 (3H, m),
2.29 (3H, s), 2.48-2.52 (1H, m), 1.66-1.69 (1H, m), 2.95-2.98 (2H, m),
5.50 (1H, s), 7.34 (1H, s), 7.55-7.57 (2H, m), 7.83 (1H, d, J=7.3Hz),
9.83 (1H, brs), 12.32 (1H, brs).

Example 1039

4-(2-Bromo-3-cyanophenyl)-6-(1-t-butoxycarbonylpiperidin-3-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl nipecotate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MP: 238°C.

Anal. Calcd. For: $C_{24}H_{25}BrN_6O_2$: C, 56.56; H, 4.95; N, 16.50.

Found: C, 56.49; H, 4.85; N, 16.50.

10 MS (EI): 509 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.37 and 1.39 (9H, s), 1.68-2.06 (4H, m), 2.65-2.75 (2H, m), 3.30-3.32 (1H, m), 3.94-3.97 (2H, m), 5.47 and 5.49 (1H, s), 7.34 (1H, s), 7.58-7.61 (2H, m), 7.82-7.86 (1H, m), 9.89 (1H, brs), 12.31 (1H, brs).

15 **Example 1040**

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(piperidin-3-yl)-2H-pyrazolo[3,4-b]pyridine trifluoroacetate

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-6-(1-t-butoxycarbonylpiperidin-3-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1021.

MP: 225°C.

Anal. Calcd. For: $C_{19}H_{17}BrN_6CF_3COOH$: C, 48.20; H, 3.47; N, 16.06.

Found: C, 47.98; H, 3.52; N, 15.97.

25 MS (EI): 409 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.68-1.98 (4H, m), 2.65-2.68 (1H, m), 3.21-3.33 (4H, m), 5.50 (1H, s), 7.35 (1H, s), 7.55-7.66 (2H, m), 7.84-7.87 (1H, m), 8.54 (1H, br), 8.96 (1H, br), 9.96 (1H, brs), 12.36 (1H, br).

30 **Example 1041**

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromo-3-cyano-

phenyl)-5-cyano-4,7-dihydro-6-(piperidin-3-yl)-2H-pyrazolo-
[3,4-b]pyridine trifluoroacetate in the same manner as in
Example 1003.

MP:174°C.

5 MS (EI):423 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.54-1.78 (4H, m), 2.18-2.20 (1H, m),
2.20 (3H, s), 2.55-2.58 (2H, m), 2.94-2.96 (1H, m), 3.31-3.34 (1H, m),
5.47 (1H, s), 7.33 (1H, s), 7.57-7.58 (2H, m), 7.84 (1H, d, J=7.3Hz),
10.06 (1H, brs), 12.29 (1H, brs).

10 **Example 1042**

4-(2-Bromo-3-cyanophenyl)-6-(1-t-butoxycarbonylpiperidin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl pipercolinate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same

15 manner as in Example 1001.

MS (EI):509 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.35 (9H, s), 1.34-1.90 (6H, m),
3.48-3.52 (2H, m), 4.42-4.48 (1H, m), 5.43 and 5.46 (1H, s), 7.36-
7.39 (1H, m), 7.53-7.57 (2H, m), 7.80-7.83 (1H, m), 9.68 and

20 9.82 (1H, brs), 12.26 (1H, brs).

Example 1043

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(piperidin-2-yl)-2H-pyrazolo[3,4-b]pyridine trifluoroacetate

The title compound was prepared from 4-(2-bromo-3-cyano-
25 phenyl)-6-(1-t-butoxycarbonylpiperidin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in
Example 1021.

MP:232°C.

MS (EI):409 (M⁺).

30 ¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.27-1.98 (5H, m), 2.47-2.51 (2H, m),
3.12-3.18 (1H, m), 4.7-4.10 (1H, m), 4.50-4.57 (1H, m), 7.40-
7.63 (3H, m), 7.79-7.82 (2H, m), 8.06 (1H, br), 10.93 (1H, brs),
12.41 (1H, brs).

Example 1044

4-(2-Bromo-3-cyanophenyl)-6-(4-t-butoxycarbonylmorpholin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl morpholine-2-carboxylate, 2-bromo-3-cyanobenzaldehyde and 3-amino-pyrazole in the same manner as in Example 1001.

MP:219°C.

MS(EI):511(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.40 (9H, s), 2.97-3.10 (2H, m),
10 3.47-3.53 (1H, m), 3.77-3.94 (3H, m), 4.37-4.39 (1H, m), 5.52 and
5.54 (1H, s), 7.34-7.36 (1H, m), 7.58-7.65 (2H, m), 7.94-7.96 (1H, m),
9.87 and 9.92 (1H, brs), 12.33 (1H, brs).

Example 1045

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(morpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine trifluoroacetate

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-6-(4-t-butoxycarbonylmorpholin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1021.

20 MP:236°C.

MS(EI):411(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.02-3.05 (1H, m), 3.24-3.33 (3H, m),
3.80-3.84 (1H, m), 4.08-4.11 (1H, m), 4.82-4.85 (1H, m), 5.55 (1H, s),
7.36 (1H, s), 7.55-7.62 (2H, m), 7.84-7.87 (1H, m), 9.14 (2H, br),
25 10.04-10.09 (1H, brs), 12.40 (1H, brs).

Example 1046

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(4-methylmorpholin-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(morpholin-2-yl)-2H-pyrazolo-
30 [3,4-b]pyridine trifluoroacetate in the same manner as in Example 1003.

MP:180°C.

MS (EI) : 425 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 2.18-2.20 (1H, m), 2.20 and 2.21 (3H, s), 2.26-2.29 (1H, m), 2.58-2.62 (1H, m), 2.75-2.78 (1H, m), 3.58-3.62 (1H, m), 3.88-3.91 (1H, m), 4.48-4.50 (1H, m), 5.51 (1H, s),
5 7.35 (1H, s), 7.56-7.61 (2H, m), 7.84-7.86 (1H, m), 9.81 and 9.84 (1H, brs), 12.31 (1H, brs) .

Example 1047

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

10 The title compound was prepared from ethyl 1,2,3,6-tetrahydropyridine-4-carboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001, and Example 1002 followed.

MP: 226°C.

15 MS (EI) : 407 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 2.36-2.40 (2H, m), 2.95-2.98 (2H, m), 3.56-3.60 (3H, m), 5.51 (1H, s), 6.15 (1H, s), 7.34 (1H, s), 7.56-7.60 (2H, m), 7.84 (1H, d, $J=7.3\text{Hz}$), 9.93 (1H, brs), 12.32 (1H, brs) .

Example 1048

20 4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1,2,3,6-tetrahydropyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in

25 Example 1003.

MP: 233°C.

MS (EI) : 421 (M^+) .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm) : 2.31 (3H, s), 2.56-2.67 (4H, m), 3.00-3.03 (2H, m), 5.50 (1H, s), 6.10 (1H, s), 7.34 (1H, s), 7.58-
30 7.60 (2H, m), 7.83 (1H, d, $J=7.3\text{Hz}$), 9.91 (1H, brs), 12.29 (1H, brs) .

Example 1049

4-(2-Bromo-3-cyanophenyl)-6-((N-t-butoxycarbonyl-N-methyl-amino)methyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from glycine ethyl ester hydrochloride, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1015.

MS(EI): 469 (M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.39 (9H, s), 2.85 (3H, s), 4.15-4.18 (2H, m), 5.49 (1H, s), 7.37 (1H, s), 7.56-7.57 (2H, m), 7.83 (1H, d, J=7.3Hz), 9.78-9.93 (1H, br), 12.31 (1H, brs).

Example 1050

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-((N-methyl-10 amino)methyl)-2H-pyrazolo[3,4-b]pyridine trifluoroacetate

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-6-((N-t-butoxycarbonyl-N-methylamino)methyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1021.

15 MP: 258°C.

MS(EI): 369 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.10 (3H, s), 4.46-4.66 (2H, m), 5.50 (1H, s), 7.47-7.48 (2H, m), 7.65 (1H, s), 7.80-7.81 (2H, m), 8.09 (1H, br), 10.81 (1H, brs), 12.38 (1H, brs).

20 **Example 1051**

6-(1-Acetylpiperidin-4-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from acetyl chloride, ethyl isonipecotate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole 25 in the same manner as in Example 1025.

MP: >280°C.

MS(EI): 451 (M⁺).

30 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.63-1.82 (3H, m), 1.98-2.00 (1H, m), 2.00 (3H, s), 2.49-2.51 (1H, m), 2.94-3.10 (2H, m), 3.89-3.91 (1H, m), 4.48-4.50 (1H, m), 5.47 (1H, s), 7.34 (1H, s), 7.56-7.58 (2H, m), 7.84 (1H, d, J=7.3Hz), 9.81 (1H, brs), 12.27 (1H, brs).

Example 1052

6-(1-Benzoylpiperidin-4-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-

4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from benzoyl chloride, ethyl isonipecotate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1025.

5 MP:>280°C.

MS (FAB): 514 (M⁺+1).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.64-2.04 (4H, m), 2.76-2.80 (1H, m),
3.05-3.10 (2H, m), 3.60-3.63 (1H, m), 4.62-4.65 (1H, m), 5.48 (1H, s),
7.34-7.58 (8H, m), 7.84 (1H, d, J=7.3Hz), 9.90 (1H, brs),
10 12.31 (1H, brs).

Example 1053

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methanesulfonylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methanesulfonyl
15 chloride, ethyl isonipecotate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1025.

MP:>280°C.

MS (EI): 487 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.75-2.07 (4H, m), 2.76-2.79 (2H, m),
20 2.89 (3H, s), 3.66-3.69 (2H, m), 5.48 (1H, s), 7.34 (1H, s), 7.56-
7.58 (2H, m), 7.84 (1H, d, J=7.3Hz), 9.84 (1H, brs), 12.30 (1H, brs).

Example 1054

6-(1-t-Butoxycarbonylpiperidin-4-yl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from ethyl isonipecotate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MP:>280°C.

Anal. Calcd. For: C₂₃H₂₆ClN₅O₂: C, 62.79; H, 5.96; N, 15.92.

30 Found: C, 62.81; H, 5.87; N, 16.01.

MS (EI): 439 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.41 (9H, s), 1.58-1.67 (2H, m),
1.86-1.91 (2H, m), 2.84-2.90 (3H, m), 4.06-4.09 (2H, m), 5.35 (1H, s),

7.21-7.33 (4H,m), 7.42 (1H,d,J=7.3Hz), 9.69 (1H,brs),
12.18 (1H,brs).

Example 1055

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from 6-(1-t-butoxy-carbonylpiperidin-4-yl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

10 MP:221°C.

MS (EI): 339 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.84-1.92 (2H,m), 2.10-2.16 (2H,m),
2.96-3.00 (3H,m), 3.30-3.40 (2H,m), 5.36 (1H,s), 7.22-7.33 (4H,m),
7.42 (1H,d,J=7.2Hz), 8.56 (1H,br), 9.76 (1H,brs), 12.26 (1H,brs).

15 **Example 1056**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-
yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]-
20 pyridine trifluoroacetate in the same manner as in Example 1003.

MP:>270°C.

Anal.Calcd.For:C₁₉H₂₀ClN₅:C, 64.49;H, 5.70;N, 19.79.

Found:C, 64.71;H, 5.68;N, 19.59.

25 MS (EI): 353 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.56-1.65 (2H,m), 1.84-1.90 (2H,m),
2.02-2.06 (2H,m), 2.16 (3H,s), 2.60-2.65 (1H,m), 2.85-2.88 (2H,m),
5.34 (1H,s), 7.21-7.33 (4H,m), 7.41 (1H,d,J=7.3Hz), 9.63 (1H,brs),
12.17 (1H,brs).

30 **Example 1057**

2-Acetyl-6-(1-acetylpiperidin-4-yl)-4-(2-chlorophenyl)-5-
cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-

(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine (1.0 g) in pyridine (1.2 mL) was added acetic anhydride (0.42 mL) at room temperature and the mixture was stirred for two hours. The mixture was evaporated under reduced pressure and the residue was washed with methanol and the precipitated crystals were collected by filtration to give the title compound (0.6 g) as colorless crystals.

MS(EI): 423 (M⁺).

¹H-NMR (400 MHz, DMSO-d₆) δ (ppm): 1.58-1.70 (2H, m), 1.91-1.96 (1H, m), 1.99-2.00 (1H, m), 2.02 (3H, s), 2.51 (3H, s), 2.55-2.58 (1H, m), 3.11-3.18 (2H, m), 3.91-3.94 (1H, m), 4.49-4.52 (1H, m), 5.37 (1H, s), 7.32-7.37 (3H, m), 7.48 (1H, d, J=7.3 Hz), 7.84 (1H, s), 10.24 (1H, brs).

Example 1058

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-oxocyclohexan-1-yl)-2H-pyrazolo[3,4-b]pyridine

To a solution of ethyl 2-cyclohexanonecarboxylate (25 g) in toluene (200 mL) was added ethyleneglycol (10.1 g) and p-toluenesulfonic acid (2.8 g) at room temperature and the mixture was heated under reflux with Dean-Stark apparatus for five hours. The reaction mixture was cooled to room temperature, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give ethyl 1,4-dioxa-spiro[4,5]decane-6-carboxylate (31 g) as a colorless oil. To a solution of acetonitrile (7.2 g) in THF (700 mL) was added n-BuLi (160 mmol) at -78°C. Further, ethyl 1,4-dioxa-spiro[4,5]decane-6-carboxylate (31 g) was added and the mixture was stirred for an hour. After acidification with hydrochloric acid, the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-cyano-2-(1,4-dioxa-spiro[4,5]decan-6-yl)ethan-2-one (14.5 g) as a colorless

oil. A solution of 2,1,3-benzoxadiazole-4-aldehyde (0.8 g), 3-aminopyrazole (0.5 g) and 1-cyano-2-(1,4-dioxaspiro[4,5]decan-6-yl)ethan-2-one (1.2 g) in acetonitrile (10 mL) was heated under reflux overnight. The reaction mixture was cooled
5 to room temperature, and the precipitated crystals were collected by filtration to give 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1,4-dioxaspiro[4,5]decan-6-yl)-2H-pyrazolo[3,4-b]pyridine (1.3 g) as colorless crystals.

To a solution of 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-
10 dihydro-6-(1,4-dioxaspiro[4,5]decan-6-yl)-2H-pyrazolo[3,4-b]pyridine (1.0 g) in methanol (30 mL) was added 4N HCl dioxane solution (6.0 mL) at room temperature and the mixture was heated at 60°C for two hours. After alkalification with sodium bicarbonate, the mixture was extracted with chloroform.
15 The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (20 mg) as colorless crystals.

MP: >270°C.

20 MS (EI): 360 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.74-1.80 (5H, m), 2.60-2.65 (3H, m), 3.31-3.35 (1H, m), 5.98 (1H, s), 6.92 (1H, d, $J=6.6\text{Hz}$), 7.39 (1H, s), 7.47 (1H, dd, $J=9.0\text{Hz}$ and 6.6Hz), 7.84 (1H, d, $J=9.0\text{Hz}$), 9.33 (1H, brs), 12.15 (1H, brs).

25 **Example 1059**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-oxocyclohexan-1-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 4-cyclohexanonecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and
30 3-aminopyrazole in the same manner as in Example 1058.

MS (FAB): 361 (M^++1).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.96-2.12 (3H, m), 2.22-2.30 (3H, m), 2.48-2.51 (1H, m), 3.27-3.31 (2H, m), 5.42 (1H, s), 7.26 (1H, s),

7.38-7.46 (1H,m), 7.57-7.61 (1H,m), 7.88-7.95 (1H,m),
9.76 (1H,brs), 12.16 (1H,br).

Example 1060

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
5 oxocyclopentan-1-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 2-cyclopentanonecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1058.

MS (FAB): 347 ($M^+ + 1$).

10 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.60-1.63 (2H,m), 1.86-2.05 (2H,m),
2.31-2.34 (2H,m), 3.43-3.46 (1H,m), 5.47 (1H,s), 7.25 and
7.30 (1H,s), 7.39-7.46 (1H,m), 7.56-7.60 (1H,m), 7.91-7.94 (1H,m),
9.90 (1H,brs), 12.20 (1H,brs).

Example 1061

15 6-Acetylmethyl-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl acetoacetate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1058.

20 MP: 200°C.

MS (FAB): 321 ($M^+ + 1$).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.22 (3H,s), 3.63-3.66 (2H,m),
5.48 (1H,s), 7.30 (1H,s), 7.47 (1H,d, J=6.6Hz), 7.61 (1H,dd, J=9.0Hz
and 6.6Hz), 7.94 (1H,d, J=9.0Hz), 10.00 (1H,brs), 12.21 (1H,brs).

25 **Example 1062**

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(2-
oxocyclohexan-1-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 2-cyclohexanonecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-
30 aminopyrazole in the same manner as in Example 1058.

MP: 273°C.

MS (EI): 422 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.72-1.81 (5H,m), 2.59-2.65 (3H,m),

3.30-3.32 (1H,m), 5.91 (1H,s), 7.05 (1H,d,J=7.3Hz), 7.40-7.43 (2H,m), 7.52 (1H,s), 7.74 (1H,d,J=7.3Hz), 9.33 (1H,brs), 12.24 (1H,brs).

Example 1063

5 6-Acetylmethyl-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl acetoacetate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1058.

10 MP:230°C.

MS (EI):382 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 2.23 (3H,s), 3.60-3.67 (2H,m), 5.50 (1H,s), 7.39 (1H,s), 7.60 (1H,dd,J=7.3Hz and 7.2Hz), 7.70 (1H,d,J=7.3Hz), 7.83 (1H,d,J=7.3Hz), 9.97 (1H,brs),

15 12.29 (1H,brs).

Example 1064

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(1-*t*-butoxy-carbonylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine (2.0 g) was added to 4N-HCl dioxane solution (20 mL) at 0°C and the mixture was stirred for an hour. The solvent was evaporated under reduced pressure and the residue was washed by ethanol, and the precipitated crystals were collected by filtration to give
25 the title compound (1.2 g) as yellow crystals.

MS (EI):339 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.83-1.90 (2H,m), 2.07-2.15 (2H,m), 2.94-2.97 (3H,m), 3.34-3.37 (2H,m), 5.36 (1H,s), 7.22-7.33 (4H,m), 7.42 (1H,d,J=7.3Hz), 8.41 (1H,br), 9.17 (1H,br), 9.77 (1H,brs),

30 12.27 (1H,brs).

Example 1065

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 4-(2,1,3-benzoxa-diazol-4-yl)-6-(1-t-butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1064.

5 MP:>270°C.

Anal. Calcd. For: C₁₈H₁₇N₇OHCl: C, 56.09; H, 5.20; N, 24.10.

Found: C, 55.80; H, 5.00; N, 23.80.

MS (EI): 347 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.82-1.85 (2H, m), 2.14-2.20 (2H, m),
10 2.93-2.99 (3H, m), 3.34-3.36 (2H, m), 5.40 (1H, s), 7.27 (1H, s),
7.43 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=9.0Hz and 6.6Hz),
7.92 (1H, d, J=9.0Hz), 8.44 (1H, br), 9.21 (1H, br), 9.87 (1H, brs),
12.25 (1H, brs).

Example 1066

15 4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine Hydrochloride

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-6-(1-t-butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in
20 Example 1064.

MP:>270°C.

MS (EI): 409 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.84-1.92 (2H, m), 2.07-2.10 (2H, m),
2.92-2.98 (5H, m), 5.48 (1H, s), 7.34 (1H, s), 7.57-7.59 (2H, m),
25 7.84 (1H, dd, J=7.3Hz and 7.2Hz), 8.30 (1H, br), 9.04 (1H, br),
9.90 (1H, brs), 12.35 (1H, br).

Example 1067

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-(1-t-butoxycarbonyl-pyrrolidin-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from ethyl 1-t-butoxycarbonylpyrrolidine-2-carboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MS (EI) : 495 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.47 (9H, s), 1.82-1.97 (4H, m), 2.31 (1H, m), 3.50 (1H, m), 4.53 (1H, m), 5.47 (1H, s), 7.51-7.91 (4H, m), 9.83 (1H, m), 12.26 (1H, s) .

5 **Example 1068**

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-(pyrrolidin-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-5-cyano-6-(1-t-butoxycarbonylpyrrolidin-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

MP: >240°C.

MS (EI) : 395 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.39-1.55 (1H, m), 1.97 (2H, m), 2.30 (1H, m), 3.32 (2H, m), 4.10-4.28 (1H, m), 5.41 (1H, s), 6.52 (1H, s), 7.34-7.47 (2H, m), 7.70 (1H, dd, J=8.3Hz and 9.0Hz), 11.89 (1H, brs) .

Example 1069

20 4-(2,1,3-Benzoxadiazol-4-yl)-6-(1-t-butoxycarbonylpyrrolidin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 1-t-butoxycarbonylpyrrolidine-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1001.

25 MS (EI) : 433 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.40 (9H, s), 1.78-1.89 (4H, m), 2.11-2.31 (1H, m), 3.72 (1H, m), 4.53 (1H, m), 5.40 (1H, s), 7.26 (1H, s), 7.30-7.40 (1H, m), 7.58 (1H, dd, J=6.4Hz and 9.6Hz), 7.91 (1H, d, J=9.6Hz), 9.86 (1H, s), 12.16 (1H, s) .

30 **Example 1070**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(pyrrolidin-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-

4-yl)-6-(1-t-butoxycarbonylpyrrolidin-2-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

MP:>240°C.

5 MS (EI) : 333 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.41-1.46 (1H, m), 1.97-2.14 (4H, m), 3.72 (1H, m), 4.11-4.32 (1H, m), 5.52 (1H, s), 7.00 (1H, s), 7.26 (1H, s), 7.30-7.42 (1H, m), 7.58 (1H, dd, J=6.4Hz and 9.6Hz), 7.91 (1H, d, J=9.3Hz), 11.87 (1H, s).

10 **Example 1071**

6-(1-t-Butoxycarbonylpyrrolidin-2-yl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 1-t-butoxycarbonylpyrrolidine-2-carboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MS (EI) : 425 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.36 (9H, s), 1.86 (4H, m), 2.32 (1H, m), 3.54 (1H, m), 4.57 (1H, m), 5.38 (1H, s), 7.23-7.27 (4H, m), 7.42 (1H, d, J=7.6Hz), 9.68 (1H, s), 12.17 (1H, s).

20 **Example 1072**

6-(1-t-Butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-(2,3-(methylenedioxy)phenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl 1-t-butoxycarbonylpiperidine-4-carboxylate, 2,3-(methylenedioxy)benzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MS (EI) : 449 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 1.39 (1H, m), 1.97-2.13 (2H, m), 2.00 (2H, m), 2.78-3.15 (2H, m), 3.31 (1H, m), 3.96 (2H, s), 5.03 (1H, d, J=9.5Hz), 6.00-6.02 (1H, m), 6.64 (1H, d, J=2.9Hz), 6.78 (1H, d, J=1.7Hz), 7.29 (1H, s), 9.46 (1H, s), 12.18 (1H, s).

Example 1073

5-Cyano-4,7-dihydro-4-(2,3-(methylenedioxy)phenyl)-6-

(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 6-(1-t-butoxy-carbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-(2,3-(methylenedioxy)phenyl)-2H-pyrazolo[3,4-b]pyridine in the same
5 manner as in Example 1002.

MS (EI) : 390 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 1.27-1.88 (5H, m), 2.49-2.96 (5H, m),
5.02 (1H, s), 6.00-6.02 (2H, m), 6.66 (1H, m), 6.76 (2H, m),
7.27 (1H, s), 9.98 (1H, s), 12.14 (1H, s).

10 **Example 1074**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]-
pyridine-6-carboxylic acid phenylamide

The title compound was prepared from N-phenyloxamic acid ethyl ester, 2-chlorobenzaldehyde and 3-aminopyrazole in the
15 same manner as in Example 1001.

MS (EI) : 375 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 5.50 (1H, s), 7.13 (1H, dd, J=7.1Hz
and 7.6Hz), 7.25-7.46 (7H, m), 7.66 (2H, dd, J=8.3Hz), 10.4 (1H, s),
10.76 (1H, s), 12.3 (1H, s).

20 **Example 1075**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine-6-carboxylic acid phenylamide

The title compound was prepared from N-phenyloxamic acid ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-
25 aminopyrazole in the same manner as in Example 1001.

MS (EI) : 383 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ (ppm) : 5.59 (1H, s), 7.11-7.15
(1H, dd, J=7.3Hz and 7.6Hz), 7.33-7.36 (3H, m), 7.51 (1H, d, J=6.6Hz),
7.63-7.68 (3H, m), 7.96 (1H, d, J=9.0Hz), 10.52 (1H, s), 10.76 (1H, s),
30 12.3 (1H, s).

Example 1076

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-[4-(naphthalen-1-
yl)piperazin-1-yl]methyl-2H-pyrazolo[3,4-b]pyridine

trihydrochloride

4-(2-Chlorophenyl)-5-cyano-6-(*t*-butyldimethylsilyloxy)methyl-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine was prepared from ethyl *t*-butyldimethylsilyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001. To a solution of 4-(2-chlorophenyl)-5-cyano-6-(*t*-butyldimethylsilyloxy)methyl-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine (20 g) in tetrahydrofuran (200 mL) was added a THF solution (49.9 mL) of 1.0 M tetrabutylammonium fluoride and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added ethyl acetate (800 mL), and the resulting mixture was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine (12.7 g) as a white solid. To a solution of 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine (12.7 g) and carbon tetrabromide (15.4 g) in methylene chloride (340 mL) was added triphenylphosphine (12.2 g) in methylene chloride (100 mL) under ice-cooling and the mixture was stirred at room temperature for 13 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine (3.84 g) as a pale-yellow solid. To a suspension of sodium hydride (60 mg) in DMF (10 mL) was added 1-(naphthalen-1-yl)piperazine (334 mg) and the mixture was stirred under ice-cooling for 30 minutes. To this reaction mixture was added a solution of 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine (500 mg) under ice-cooling and the mixture was stirred under ice-

cooling for 6 hours. To the reaction mixture was added water and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was
5 evaporated and the obtained residue was purified by silica gel column chromatography (eluent: ethyl acetate-methanol (1:1)). The obtained oil was treated with hydrogen chloride-methanol to give the title compound (370 mg) as white crystals.

MP:203-205°C (decomposition)

10 MS(EI):481(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.31-3.70(8H, m), 4.33(2H, m), 4.85(3H, m), 5.54(1H, s), 7.19(1H, d, J=7.3Hz), 7.29-7.54(8H, m), 7.67(1H, d, J=8.1Hz), 7.92(1H, d, J=7.1Hz), 8.15(1H, d, J=7.3Hz), 10.35(1H, s), 11.28(1H, brs).

15 **Example 1077**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(4-methyl-homopiperazin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

The title compound was prepared from 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine and
20 N-methylhomopiperazine in the same manner as in Example 1076.

MP:204-206°C (decomposition)

MS(EI):382(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.22(2H, m), 2.78(3H, s), 3.24-
25 4.11(12H, m), 5.48(1H, s), 7.14-7.35(4H, m), 7.45(1H, d, J=8.0Hz), 10.17(1H, brs), 11.51(1H, brs).

Example 1078

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(4-phenylpiperazin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine trihydrochloride

30 The title compound was prepared from 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine and 1-phenylpiperazine in the same manner as in Example 1076.

MP:217-220°C (decomposition)

MS (EI) : 430 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 3.20-4.00 (9H, m), 4.27 (2H, m),
5.51 (1H, s), 6.86 (1H, t, J=7.1Hz), 7.01 (2H, d, J=8.0Hz), 7.24-
7.39 (6H, m), 7.45 (1H, d, J=9.9Hz), 9.50 (1H, brs), 10.37 (1H, s),
5 11.40 (1H, brs) .

Example 1079

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-phthalimidomethyl-2H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-
10 4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.8 g) in DMF (10 mL)
was added potassium phthalimide (445 mg) under ice-cooling and
the mixture was stirred under ice-cooling for 4 hours. To the
reaction mixture was added water and the mixture was extracted
with ethyl acetate. The extract was washed with a saturated
15 aqueous sodium chloride solution and dried over anhydrous
magnesium sulfate. The solvent was evaporated and the obtained
residue was purified by silica gel column chromatography
(eluent: ethyl acetate-hexane (2:1)) to give the title
compound (285 mg) as white crystals.

20 MP: >250°C

MS (EI) : 416 (M⁺) .

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 4.66 (2H, d, J=2.4Hz), 5.40 (1H, s),
7.24-7.45 (5H, m), 7.82-7.94 (4H, m), 10.04 (1H, s), 12.23 (1H, s) .

Example 1080

25 6-Acetyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(1,1-
dimethoxyethyl)-2H-pyrazolo[3,4-b]pyridine was prepared from
methyl 2,2-dimethoxypropionate, 2-chlorobenzaldehyde and 3-
30 aminopyrazole in the same manner as in Example 1001. To a
solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(1,1-
dimethoxyethyl)-2H-pyrazolo[3,4-b]pyridine (1.0 g) in
dichloromethane (10 mL) was added a trifluoroacetic acid (10

mL) under ice-cooling and the mixture was stirred under ice-cooling for 1 hour. The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give the title compound (370 mg) as white crystals.

5 MP: 225-228°C (decomposition)

MS(EI): 298 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.56 (3H, s), 5.49 (1H, s), 7.25-7.36 (4H, m), 7.45 (1H, d, $J=7.8\text{Hz}$), 10.12 (1H, s), 12.50 (1H, brs).

Example 1081

10 6-Acetyl-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-bromo-3-cyanobenzaldehyde, 3-aminopyrazole and methyl 2,2-dimethoxypropionate in the same manner as in Example 1001.

15 MP: >230°C

MS(EI): 368 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.42 (3H, s), 5.54 (1H, s), 7.32 (1H, brs), 7.50-7.59 (2H, m), 7.80 (1H, dd, $J=1.7\text{Hz}$ and 7.3Hz), 10.19 (1H, s), 12.39 (1H, brs).

20 **Example 1082**

6-Acetyl-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and methyl 2,2-dimethoxypropionate
25 in the same manner as in Example 1001.

MP: 230°C (decomposition)

MS(EI): 306 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.55 (3H, s), 5.54 (1H, s), 7.33 (1H, s), 7.49 (1H, d, $J=6.6\text{Hz}$), 7.61 (1H, dd, $J=6.6\text{Hz}$ and 8.6Hz),
30 7.96 (1H, d, $J=9.2\text{Hz}$), 10.27 (1H, s), 12.36 (1H, brs).

Example 1083

6-(1-Benzyl-2-oxopyrrolidin-4-yl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl 1-benzyl-2-oxopyrrolidine-4-carboxylate in the same manner as in Example 1001.

MP: >230°C

5 Anal. Calcd. for: $C_{24}H_{20}ClN_5O$: C, 67.05; H, 4.69; N, 16.29.

Found: C, 66.86; H, 4.56; N, 16.31.

MS (EI): 429 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.60 (1H, dd, $J=9.5$ Hz and 16.4Hz),
2.81 (1H, dd, $J=10.5$ Hz and 16.4Hz), 3.39 (1H, m), 3.47 (1H, m),
10 4.42 (2H, m), 5.36 (1H, s), 7.23-7.43 (10H, m), 10.04 (1H, s),
12.21 (1H, s).

Example 1084

4-(2-Bromo-3-cyanophenyl)-5-(pyridin-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

15 To a solution of 2-picoline (10 g) in THF (75 mL) was added *n*-BuLi (113 mmol) at -40°C. Further, methyl butanoate (15.8 mL) was added and the mixture was stirred for 1 hour, and the mixture quenched with water. The mixture was extracted with ethyl acetate. The solvent was evaporated under reduced
20 pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give 2-(2-oxopentanyl)pyridine (4.8 g) as a yellow oil. A solution of 2-bromo-3-cyanobenzaldehyde (1.5 g), Meldrum's acid (1.0 g), 2-(2-oxopentanyl)pyridine (1.2 g) and ammonium acetate (0.6 g)
25 in acetic acid (7 mL) was heated under reflux for 11 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) and the obtained residue was
30 crystallized from ethyl acetate to give colorless crystals (520 mg). To a solution of dimethylformamide (384 mg) in chloroform (5 mL) were added phosphorus oxychloride (805 mg) and a solution of the obtained crystals (520 mg) under ice-

cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (3.4 g) solution was added and the mixture was stirred for 1 hour. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure to give oil. The obtained oil was purified by silica gel column chromatography (eluent: chloroform-methanol (9:1)) to give a yellow solid (530 mg). To a solution of the obtained solid in pyridine (10 mL) was added hydrazine (120 mg), and the mixture was stirred with heating for 4 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give oil. To the obtained oil was added water and the mixture was extracted with ethyl acetate. The extract was washed a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give the title compound (145 mg) as a pale-yellow crystal. MP: 205-208°C (decomposition)

Anal. Calcd. for: $C_{21}H_{18}BrN_5$: C, 60.01; H, 4.32; N, 16.66.

Found: C, 59.83; H, 4.42; N, 16.26.

MS (EI): 420 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83 (3H, t, $J=7.6$ Hz), 1.62 (2H, m), 2.24 (1H, m), 2.33 (1H, m), 5.93 (1H, s), 6.98 (1H, dd, $J=4.9$ Hz and 7.3Hz), 7.05 (1H, d, $J=7.8$ Hz), 7.28 (1H, m), 7.39 (1H, m), 7.51-7.60 (3H, m), 8.36 (1H, d, $J=3.6$ Hz), 8.52 (1H, s), 11.84 (1H, s).

Example 1085

6-(1-tert-Butoxycarbonylpyrrolidin-3-yl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

To a solution of methyl 1-benzyl-2-oxopyrrolidine-4-carboxylate (10.9 g) in THF (50 mL) was added 1.0 M borane in THF (84 mL) under ice-cooling and the mixture was refluxed for 1 hour. Decomposition of excess borane and boron complexes was effected by the dropwise addition of 30 mL of methanolic

hydrogen chloride followed by refluxing for 1 hour. After removal of the solvents under reduced pressure another 30 mL of methanolic hydrogen chloride was added, and the mixture was refluxed an additional 1 hour. The solvents were again removed
5 in *vacuo* and the residue was treated with saturated aqueous sodium hydrogencarbonate solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give methyl 1-benzyl-
10 3-pyrrolidinecarboxylate (4.8 g) as a pale yellow oil. A suspension of methyl 1-benzyl-3-pyrrolidinecarboxylate (4.8 mg), 5% palladium on carbon (300 mg) and ammonium formate (2.8 g) in methanol (50 mL)-water (5 mL) was refluxed for 2 hours. The reaction mixture was filtered through Celite and the
15 filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: chloroform-methanol (9:1)) to give methyl 3-pyrrolidinecarboxylate as a yellow oil. To a solution of methyl 3-pyrrolidinecarboxylate (1.7 g) in dichloromethane (20
20 mL) was added dimethylaminopyridine (161 mg) and di-*tert*-butyldicarbonate (3.4 g) at 0°C and the mixture was stirred for 13 hours. The mixture was evaporated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (2:1)) to give
25 methyl 1-*tert*-butoxycarbonyl-3-pyrrolidinecarboxylate (2.6 g) as a colorless oil. To a solution of acetonitrile (554 mg) in THF (30 mL) was added *n*-BuLi (12.4 mmol) at -78°C. Further, methyl 1-*tert*-butoxycarbonyl-3-pyrrolidinecarboxylate (2.6 g) in THF (10 mL) was added and the mixture was stirred for 10
30 hours and the reaction was quenched with water. The mixture was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (2:1)) to give 1-(1-*tert*-

butoxycarbonylpyrrolidin-3-yl)-2-cyanoethan-1-one (2.35 g) as a colorless oil. A solution of 2-chlorophenylaldehyde (1.4 g), 3-aminopyrazole (819 mg) and 1-(1-tert-butoxycarbonylpyrrolidin-3-yl)-2-cyanoethan-1-one (2.35 g) in
5 acetonitrile (10 mL) was heated under reflux for 1.5 hours. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (2.18 g) as colorless crystals.
Anal. Calcd. For: $C_{22}H_{24}ClN_5O_2$: C, 62.04; H, 5.68; N, 16.44.
10 Found: C, 61.94; H, 5.69; N, 16.45.
MS (EI): 425 (M^+).
 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.14 (9H, s), 2.07 (1H, m), 2.32 (1H, m), 3.29-3.58 (5H, m), 5.37 (1H, s), 7.22-7.34 (4H, m), 7.42 (1H, d, $J=8.3$ Hz), 9.78 (1H, s), 12.20 (1H, s).

15 **Example 1086**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(pyrrolidin-3-yl)-2H-pyrazolo[3,4-b]pyridine

6-(1-tert-Butoxycarbonylpyrrolidin-3-yl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (706 mg) was
20 added to 4N-HCl dioxane solution (5 mL) at room temperature and the mixture was stirred for 2 hours. The solvent was evaporated under reduced pressure and the residue was washed by ethanol-ethyl acetate, and the precipitated crystals were collected by filtration to give the title compound (460 mg) as
25 colorless crystals.

MP: 210-215°C (decomposition)

MS (EI): 325 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.24 (2H, m), 3.15 (1H, m), 3.26-3.55 (3H, m), 3.64 (1H, m), 5.34 (1H, s), 5.40 (1H, brs), 7.23-
30 7.32 (4H, m), 7.43 (1H, d, $J=7.3$ Hz), 9.38 (1H, brs), 9.51 (1H, brs), 9.97 (1H, s).

Example 1087

4-(2,1,3-Benzoxadiazol-4-yl)-5-(pyridin-2-yl)-4,7-dihydro-6-

propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, Meldrum's acid, 2-(2-oxopentanyl)pyridine and ammonium acetate in the same manner as in Example 1084.

5 MS (EI): 358 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.84 (3H, t, $J=7.3\text{Hz}$), 1.64 (2H, m), 2.27 (1H, m), 2.35 (1H, m), 5.96 (1H, s), 6.95 (1H, m), 7.11-7.18 (3H, m), 7.40 (1H, m), 7.51 (1H, m), 7.69 (1H, d, $J=9.3\text{Hz}$), 8.35 (1H, m), 8.54 (1H, s), 11.78 (1H, brs).

10 **Example 1088**

6-(1-t-Butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-(indan-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl isonipecotate, 4-indancarboxaldehyde and 3-aminopyrazole in the same manner as

15 in Example 1001.

MS (EI): 445 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.41 (9H, s), 1.56-1.59 (2H, m), 1.88-1.06 (4H, m), 2.58-2.83 (7H, m), 4.06 (2H, m), 4.96 (1H, s), 6.90 (1H, m), 7.04-7.07 (2H, m), 7.14 (1H, s), 9.55 (1H, s),
20 12.08 (1H, s).

Example 1089

6-(1-t-Butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-(2,3-dihydrobenzo[b]furan-7-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl isonipecotate, 7-(2,3-dihydrobenzo[b]furan)carboxaldehyde and 3-aminopyrazole
25 in the same manner as in Example 1001.

MS (EI): 445 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.42 (9H, s), 1.57-1.66 (2H, m), 1.88 (4H, m), 2.73-2.90 (3H, m), 3.17 (2H, m), 4.09 (2H, m),
30 4.54 (2H, m), 5.01 (1H, s), 6.76 (1H, m), 6.84 (1H, d, $J=7.1\text{Hz}$), 7.05 (1H, d, $J=6.6\text{Hz}$), 7.22 (1H, s), 9.52 (1H, s), 12.06 (1H, s).

Example 1090

6-(1-t-Butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-

(3,4-dihydro-2H-benzopyran-8-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl isonipecotate, 8-(3,4-dihydro-2H-benzopyrane)carboxaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

5 MS(EI): 461 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.42 (9H, s), 1.58-1.69 (2H, m), 1.80-2.00 (4H, m), 2.73-2.95 (5H, m), 4.09 (2H, m), 4.22 (2H, m), 5.14 (1H, s), 6.74 (1H, m), 6.84-6.89 (2H, m), 7.21 (1H, s), 9.48 (1H, s), 12.03 (1H, s).

10 **Example 1091**

6-(1-t-Butoxycarbonylpiperidin-4-yl)-4-(2-chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl isonipecotate, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MS(EI): 461 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.41 (9H, s), 1.62 (2H, m), 1.89 (2H, m), 2.60-2.90 (3H, m), 4.10 (2H, m), 5.54 (1H, s), 7.32 (1H, s), 7.52-7.56 (2H, m), 7.75 (1H, d, J=9.3Hz), 9.79 (1H, s), 12.25 (1H, s).

Example 1092

5-Cyano-4,7-dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 6-(1-t-butoxycarbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.

MS(EI): 361 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.83-1.98 (4H, m), 2.14 (2H, m), 2.74 (2H, m), 2.90-3.00 (3H, m), 4.22 (2H, m), 3.40-3.70 (5H, m), 4.16-4.27 (2H, m), 5.15 (1H, s), 6.74 (1H, m), 6.83-6.89 (2H, m), 7.22 (1H, s), 9.54 (1H, s).

Example 1093

5-Cyano-4,7-dihydro-4-(indan-4-yl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 6-(1-t-butoxy-carbonylpiperidin-4-yl)-5-cyano-4,7-dihydro-4-(indan-4-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1002.
MS(EI): 345(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.80-1.99(4H, m), 2.14(2H, m), 2.58(1H, m), 2.82-2.95(6H, m), 3.30-3.50(2H, m), 4.97(1H, s), 6.90(1H, m), 7.04-7.09(2H, m), 7.17(1H, s), 8.37(1H, m),
10 9.10(1H, m), 9.62(1H, s), 12.18(1H, brs).

Example 1094

5-Cyano-4,7-dihydro-4-(indan-4-yl)-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-4-(indan-4-yl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride in the same manner as in Example 1003.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.56(2H, m), 1.84-1.98(6H, m), 2.15(2H, m), 2.58(1H, m), 2.80-3.00(6H, m), 3.20-3.40(2H, m), 4.95(1H, s), 6.90(1H, m), 7.05-7.07(2H, m), 7.14(1H, s),
20 9.54(1H, brs), 12.10(1H, brs).

Example 1095

5-Cyano-4,7-dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine Hydrochloride

The title compound was prepared from 5-cyano-4,7-dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride in the same manner as in Example 1003.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.90-2.00(4H, m), 2.24(2H, m), 2.73-2.75(5H, m), 2.94-3.08(3H, m), 3.40-3.48(2H, m), 4.17-
30 4.27(2H, m), 5.15(1H, s), 6.74(1H, m), 6.84-6.89(2H, m), 7.22(1H, s), 9.58(1H, s), 9.80(1H, m), 12.15(1H, s).

Example 1096

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-

methanesulfonylpiperidin-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methanesulfonyl-chloride, ethyl pipercolinate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1025.

5 MS(EI): 425(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.20-2.07(7H, m), 2.95 and 2.98(3H, s), 2.98-3.17(1H, m), 3.63-3.68(1H, m), 5.40 and 5.52(1H, s), 7.24 and 7.27(1H, s), 7.41-7.63(2H, m), 7.90-7.93(1H, m), 9.80 and 9.82(1H, brs), 12.16(1H, brs).

10 **Example 1097**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1064.
15 MS(EI): 361(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.86-1.90(2H, m), 2.24-2.27(2H, m), 2.48(3H, s), 2.72-2.75(2H, m), 2.94-2.98(2H, m), 3.20-3.33(1H, br), 3.44-3.47(1H, m), 5.40(1H, s), 7.28(1H, s),
20 7.44(1H, d, J=6.6Hz), 7.59(1H, dd, J=9.0Hz and 6.6Hz), 7.93(1H, d, J=9.0Hz), 9.92(1H, brs), 12.26(1H, brs).

Example 1098

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1,2-dihydro-1-methyl-2-oxo-pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine
25

The title compound was prepared from 1,2-dihydro-1-methyl-2-oxo-pyridine-4-carboxylic acid ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 1001.

30 MS(EI): 371(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 3.46(3H, s), 5.42(1H, s), 6.34(1H, d, J=7.2Hz), 6.56(1H, s), 7.33(1H, s), 7.52(1H, d, J=7.2Hz), 7.61(1H, dd, J=9.0Hz and 6.6Hz), 7.80(1H, d,

J=6.6Hz), 7.95(1H, d, J=9.0Hz), 10.33(1H, brs), 12.29(1H, brs).

Example 1099

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1,2,5,6-tetrahydropyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

5 hydrochloride

The title compound was prepared from 1,2,3,4-tetrahydropyridine-3-carboxylic acid ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

10 MS(EI): 345(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.42-2.44(2H, m), 3.11-3.14(2H, m), 3.84-3.87(2H, m), 4.39(1H, br), 5.46(1H, s), 6.36(1H, s), 7.30(1H, s), 7.49(1H, d, J=6.6Hz), 7.56(1H, dd, J=9.0Hz and 6.6Hz), 7.94(1H, d, J=9.0Hz), 9.39(2H, br), 10.06(1H, brs).

15 **Example 1100**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methyl-1,4,5,6-tetrahydropyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1,4,5,6-tetrahydropyridin-3-yl)-
20 2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.

MS(EI): 359(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.18-2.20(2H, m), 2.43-2.47(2H, m), 3.02-3.11(2H, m), 5.43(1H, s), 6.11(1H, s), 7.26(1H, s), 7.43(1H, d, J=6.6Hz), 7.59(1H, dd, J=9.0Hz and 6.6Hz),
25 7.92(1H, d, J=9.0Hz), 9.87(1H, brs), 12.16(1H, brs).

Example 1101

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-(methylamino)ethyl)-2H-pyrazolo[3,4-b]pyridine

30 2 hydrochloride

The title compound was prepared from 2-methylglycine ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Examples 1015 and 1002.

MS (EI): 321 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 1.56(3H, d, $J=6.8\text{Hz}$), 3.07(3H, s), 4.59-4.68(3H, m), 5.66(1H, s), 7.29(1H, d, $J=6.6\text{Hz}$), 7.44(1H, s), 7.52(1H, dd, $J=9.0\text{Hz}$ and 6.6Hz), 7.87(1H, d, $J=9.0\text{Hz}$), 8.22(1H, br), 8.44(1H, br), 10.95(1H, brs).

Example 1102

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1,2-dihydro-1-methyl-2-oxo-pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 1,2-dihydro-1-methyl-2-oxo-pyridine-4-carboxylic acid ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MS (EI): 433 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 3.46(3H, s), 5.35(1H, s), 6.37(1H, d, $J=7.2\text{Hz}$), 6.61(1H, s), 7.38(1H, s), 7.60(1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.72-7.86(3H, m), 10.31(1H, brs), 12.37(1H, brs).

Example 1103

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(4-(methylamino)cyclohexyl)-2H-pyrazolo[3,4-b]pyridine
2 hydrochloride

The title compound was prepared from 4-aminocyclohexanecarboxylic acid ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1015 and 1002.

MS (EI): 436 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 1.39(2H, m), 1.80-1.90(4H, m), 2.15-2.16(2H, m), 2.84-2.86(1H, m), 3.14-3.16(1H, m), 4.20(2H, br), 5.46(1H, s), 7.33(1H, s), 7.56-7.57(2H, m), 7.82(1H, d, $J=7.3\text{Hz}$), 8.98(2H, br), 9.80(1H, brs).

Example 1104

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1,2,5,6-tetrahydropyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

2 hydrochloride

The title compound was prepared from 1,2,5,6-tetrahydropyridine-3-carboxylic acid ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in
5 Examples 1001 and 1002.

MS(EI): 407 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.43-2.44 (2H, m), 3.13-3.15 (2H, m), 3.70-3.72 (2H, br), 3.86-3.88 (2H, m), 5.54 (1H, s), 6.41 (1H, s), 7.36 (1H, s), 7.58 (1H, dd, J=7.3Hz and 7.2Hz), 7.84 (1H, d,
10 J=7.3Hz), 7.86 (1H, d, J=7.3Hz), 9.32 (2H, br), 10.03 (1H, brs).

Example 1105

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(4-(dimethylamino)cyclohexyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromo-3-
15 cyanophenyl)-5-cyano-4,7-dihydro-6-(4-(methylamino)cyclohexyl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.

MS(EI): 450 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.26-1.29 (2H, m), 1.76-1.93 (6H, m), 2.27 (6H, s), 2.34-2.36 (1H, m), 2.63-2.66 (1H, m), 5.45 (1H, s), 7.33 (1H, s), 7.56-7.60 (2H, m), 7.82 (1H, d, J=7.3Hz),
20 9.74 (1H, brs), 12.27 (1H, s).

Example 1106

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methyl-1,4,5,6-tetrahydropyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine
25

The title compound was prepared from 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1,4,5,6-tetrahydropyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in
Example 1003.

30 MS(EI): 420 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.21-2.22 (2H, m), 2.28 (3H, s), 2.48-2.49 (2H, m), 3.08-3.12 (2H, m), 5.49 (1H, s), 6.15 (1H, s), 7.33 (1H, s), 7.56-7.61 (2H, m), 7.84 (1H, dd, J=7.3Hz and 7.2Hz),

9.87(1H, brs), 12.26(1H, brs).

Example 1107

6-(exo-2-Azabicyclo[2,2,2]octan-6-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 2 hydrochloride

The title compound was prepared from exo-2-azabicyclo[2,2,2]octane-6-carboxylic acid ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

10 MS(EI): 373(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.53-1.55(1H, m), 1.75-1.77(1H, m), 1.89-2.06(4H, m), 2.21-2.23(1H, m), 3.07-3.10(2H, m), 3.43-3.48(4H, m), 5.39-5.43(1H, s), 7.26-7.28(1H, m), 7.44-7.47(1H, m), 7.57-7.61(1H, m), 7.93-7.95(1H, m), 8.87-9.03(1H, br), 9.46-9.52(1H, br), 9.73 and 9.80(1H, brs).

Example 1108

6-(endo-2-Azabicyclo[2,2,2]octan-6-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 2

Hydrochloride

20 The title compound was prepared from endo-2-azabicyclo[2,2,2]octane-6-carboxylic acid ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 373(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.67-1.73(3H, m), 2.03-2.13(4H, m), 3.04-3.06(1H, m), 3.34-3.57(5H, m), 5.49(1H, s), 7.30(1H, s), 7.50-7.51(1H, m), 7.58-7.60(1H, m), 7.92-7.94(1H, m), 8.07(1H, br), 9.79(1H, br), 9.89(1H, br).

Example 1109

30 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(exo-2-methyl-2-azabicyclo[2,2,2]octan-6-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 6-(exo-2-

azabicyclo[2,2,2]octan-6-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2*H*-pyrazolo[3,4-*b*]pyridine in the same manner as in Example 1003.

MS(EI): 387(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.43-1.44(1H, m), 1.70-1.90(5H, m), 2.11-2.13(1H, m), 2.38-2.46(4H, m), 3.00-3.02(1H, m), 3.32-3.36(2H, m), 5.38 and 5.40(1H, s), 7.25-7.27(1H, m), 7.38-7.42(1H, m), 7.56-7.61(1H, m), 7.90-7.93(1H, m), 9.73(1H, br), 12.23(1H, br).

10 **Example 1110**

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-(piperidin-4-yl)-2*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate
2 hydrobromide

A solution of 2,1,3-benzoxadiazole-4-aldehyde (3.0 g),
15 Meldrum's acid (3.0 g), ethyl 3-keto-3-(1-benzylcarbonylpiperidin-4-yl)propionate (6.8 g) and ammonium acetate (1.8 g) in acetic acid (20 mL) was stirred under reflux for 12 hrs. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced
20 pressure to give colorless crystals (4.7 g). To a solution of dimethylformamide (2.7 g) in chloroform (10 mL) were added phosphorus oxychloride (3.4 mL) and a solution of the obtained colorless crystals (4.7 g) in chloroform (10 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-
25 cooling, an aqueous sodium acetate (37.8 g) solution was added and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-
30 ethyl acetate (8:2)) to give colorless crystals. To a solution of the obtained colorless crystals in pyridine (20 mL) was added hydrazine (1.4 g) and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room

temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (840 mg) as colorless crystals. To a solution of the obtained colorless crystals in acetic acid (10 mL) was added HBr-AcOH solution (10 mL) and the mixture was stirred for 3 hours. The solvent was evaporated under reduced pressure to give colorless crystals. The crystal was purified by recrystallization from EtOH to give the title compound (630 mg) as colorless crystals.

MS(EI): 394 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.77(3H, t, $J=7.3\text{Hz}$), 1.80-2.16(4H, m), 2.90-2.93(2H, m), 3.40-3.43(2H, m), 3.80(2H, q, $J=7.3\text{Hz}$), 4.12-4.15(1H, m), 4.50(2H, br), 5.67(1H, s), 7.17(1H, d, $J=6.6\text{Hz}$), 7.26(1H, s), 7.51(1H, dd, $J=9.0\text{Hz}$ and 6.6Hz), 7.79(1H, d, $J=9.0\text{Hz}$), 8.10(1H, br), 8.74(1H, br), 9.38(1H, brs).

Example 1111

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(endo-2-methyl-2-azabicyclo[2,2,2]octan-6-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 6-(endo-2-azabicyclo[2,2,2]octan-6-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.

MS(EI): 387 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.43-1.47(2H, m), 1.60-1.64(2H, m), 1.81-1.82(1H, m), 1.79-2.06(2H, m), 2.24-2.26(1H, m), 2.36(3H, s), 2.76-2.80(2H, m), 3.19-3.22(1H, m), 5.43(1H, s), 7.25(1H, s), 7.42-7.46(1H, m), 7.57-7.60(1H, m), 7.90-7.94(1H, m), 10.79(1H, brs), 12.16(1H, brs).

Example 1112

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

2 hydrochloride

The title compound was prepared from ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate in the same manner as in

5 Example 1003.

MS(EI): 408(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.75(3H, t, J=7.3Hz), 1.55-1.56(1H, m), 1.71-1.73(1H, m), 1.87-2.06(4H, m), 2.17(3H, s), 2.84-2.87(2H, m), 3.78(2H, q, J=7.3Hz), 3.93-3.96(1H, m),
10 5.68(1H, s), 7.12(1H, d, J=6.6Hz), 7.22(1H, s), 7.49(1H, dd, J=9.0Hz and 6.6Hz), 7.77(1H, d, J=9.0Hz), 9.32(1H, brs), 12.06(1H, brs).

Example 1113

4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride
15

The title compound was prepared from ethyl nipecotate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 383(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.85-1.93(2H, m), 2.14-2.20(2H, m), 2.94-2.98(2H, m), 3.32-3.36(3H, m), 5.36(1H, s), 7.16(1H, dd, J=7.3Hz and 7.2Hz), 7.23-7.27(2H, m), 7.35(1H, dd, J=7.3Hz and 7.2Hz), 7.59(1H, d, J=7.3Hz), 8.41(1H, br), 9.14(1H, br), 9.73(1H, brs), 12.21(1H, brs).

Example 1114

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride
25

The title compound was prepared from ethyl nipecotate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as
30 in Examples 1001 and 1002.

MS(EI): 335(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.87-1.95(2H, m), 2.14-2.20(2H, m), 2.94-3.03(3H, m), 3.32-3.36(2H, m), 3.82(3H, s), 5.21(1H,

s), 6.88(1H, dd, J=7.3Hz and 7.2Hz), 6.99(1H, d, J=7.3Hz), 7.05(1H, d, J=7.3Hz), 7.15-7.20(2H, m), 8.44(1H, br), 9.17(1H, br), 9.53(1H, brs), 12.11(1H, brs).

Example 1115

5 5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from ethyl nipecotate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

10 MS(EI): 373(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.84-1.90(2H, m), 2.16-2.20(2H, m), 2.94-3.00(3H, m), 3.32-3.38(2H, m), 5.44(1H, s), 7.24-7.36(3H, m), 7.56(1H, d, J=7.3Hz), 8.52(1H, br), 9.24(1H, br), 9.79(1H, brs), 12.29(1H, brs).

15 **Example 1116**

4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2-bromophenyl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-

20 b]pyridine in the same manner as in Example 1003.

MS(EI): 397(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.56-1.63(2H, m), 1.85-1.90(2H, m), 2.01-2.06(2H, m), 2.17(3H, s), 2.62-2.65(1H, m), 2.87-2.89(2H, m), 5.34(1H, s), 7.14-7.26(3H, m), 7.36(1H, dd, J=7.3Hz and 7.2Hz), 7.60(1H, d, J=7.3Hz), 9.60(1H, brs), 12.16(1H, brs).

Example 1117

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from 5-cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 1003.

MS(EI): 349(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.56-1.66(2H, m), 1.86-1.92(2H, m), 2.01-2.04(2H, m), 2.17(3H, s), 2.64-2.67(1H, m), 2.86-2.88(2H, m), 3.84(3H, s), 5.20(1H, s), 6.90(1H, dd, J=7.3Hz and 7.2Hz), 6.98(1H, d, J=7.3Hz), 7.05(1H, d, J=7.3Hz), 7.16-7.19(2H, m), 9.41(1H, brs), 12.01(1H, brs).

Example 1118

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride in the same manner as in Example 1003.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.57-1.65(2H, m), 1.85-1.90(2H, m), 2.01-2.06(2H, m), 2.17(3H, s), 2.59-2.66(1H, m), 2.86-2.89(2H, m), 5.43(1H, s), 7.23(1H, d, J=7.3Hz), 7.29(1H, s), 7.35(1H, dd; J=7.3Hz and 7.2Hz), 7.51(1H, d, J=7.3Hz), 9.65(1H, brs), 12.18(1H, brs).

Example 1119

5-Cyano-4,7-dihydro-4-(2-fluorophenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from ethyl nipecotate, 2-fluorobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 323(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.85-1.89(2H, m), 2.12-2.20(2H, m), 2.90-2.98(3H, m), 3.33-3.39(2H, m), 5.20(1H, s), 7.14-7.28(5H, m), 8.37(1H, br), 9.09(1H, br), 9.66(1H, brs), 12.23(1H, brs).

Example 1120

5-Cyano-4-(2,3-difluorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from ethyl nipecotate, 2,3-

difluorobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 341 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 1.84-1.88 (2H, m), 2.14-2.19 (2H, m), 2.95-3.00 (3H, m), 3.33-3.38 (2H, m), 5.26 (1H, s), 7.03 (1H, d, $J=7.3\text{Hz}$), 7.18 (1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.26-7.31 (2H, m), 8.80 (2H, br), 9.74 (1H, brs), 12.29 (1H, brs).

Example 1121

5-Cyano-4-(2,6-difluorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from ethyl nipecotate, 2,6-difluorobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 341 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 1.76-1.84 (2H, m), 2.13-2.18 (2H, m), 2.91-2.95 (3H, m), 3.28-3.30 (2H, m), 5.35 (1H, s), 7.02-7.07 (2H, m), 7.31-7.38 (2H, m), 8.77 (2H, br), 9.68 (1H, brs), 12.22 (1H, brs).

Example 1122

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride

The title compound was prepared from ethyl nipecotate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 351 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 1.86-1.93 (2H, m), 2.17-2.23 (2H, m), 2.50 (3H, s), 2.95-3.00 (3H, m), 3.36-3.40 (4H, m), 5.36 (1H, s), 7.14-7.33 (5H, m), 8.49 (1H, br), 9.22 (1H, br), 9.63 (1H, brs).

Example 1123

5-Cyano-4-(2,6-dichlorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from ethyl nipecotate, 2,6-

dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 373(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.80-1.84(2H, m), 2.12-2.20(2H, m), 2.90-2.98(3H, m), 3.30-3.33(2H, m), 5.92(1H, s), 7.19(1H, s), 7.29(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz), 7.51(1H, d, J=7.3Hz), 8.41(1H, br), 9.16(1H, br), 9.73(1H, brs), 12.18(1H, brs).

Example 1124

10 5-Cyano-4,7-dihydro-6-(piperidin-4-yl)-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine
2 hydrochloride

The title compound was prepared from ethyl nipecotate, 2-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same
15 manner as in Examples 1001 and 1002.

MS(EI): 373(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.83-1.90(2H, m), 2.18-2.26(2H, m), 2.92-3.00(3H, m), 3.38-3.43(2H, m), 4.16(2H, br), 5.22(1H, s), 7.06(1H, s), 7.42-7.44(2H, m), 7.63-7.69(2H, m), 8.57(1H, br), 9.30(1H, br), 9.77(1H, br).

Example 1125

5-Cyano-4,7-dihydro-4-(2-fluorophenyl)-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-4-(2-fluorophenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine
25 hydrochloride in the same manner as in Example 1003.

MS(EI): 337(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.55-1.59(2H, m), 1.83-1.88(2H, m), 1.96-2.00(2H, m), 2.15(3H, s), 2.60-2.63(1H, m), 2.84-
30 2.88(2H, m), 5.17(1H, s), 7.13-7.24(5H, m), 9.60(1H, brs), 12.18(1H, brs).

Example 1126

5-Cyano-4-(2,3-difluorophenyl)-4,7-dihydro-6-(1-

methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4-(2,3-difluorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride in the same manner as in
5 Example 1003.

MS(EI): 355(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.55-1.59(2H, m), 1.82-1.8(2H, m), 1.99-2.02(2H, m), 2.15(3H, s), 2.57-2.60(1H, m), 2.84-2.88(2H, m), 5.23(1H, s), 7.00(1H, dd, J=7.3Hz and 7.2Hz),
10 7.16(1H, d, J=7.3Hz), 7.27-7.30(2H, m), 9.66(1H, brs), 12.24(1H, brs).

Example 1127

5-Cyano-4-(2,6-difluorophenyl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from 5-cyano-4-(2,6-difluorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride in the same manner as in Example 1003.

MS(EI): 355(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.49-1.53(2H, m), 1.82-1.86(2H, m), 1.96-2.01(2H, m), 2.15(3H, s), 2.48-2.51(1H, m), 2.83-2.86(2H, m), 5.31(1H, s), 7.00-7.05(2H, m), 7.29-7.31(2H, m), 9.60(1H, brs), 12.15(1H, brs).

Example 1128

25 5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride

The title compound was prepared from ethyl nipecotate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

30 MS(EI): 351(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.84-1.93(2H, m), 2.17-2.23(2H, m), 2.94-3.00(3H, m), 3.35-3.38(2H, m), 4.42(2H, br), 5.40(1H, s), 7.30(1H, s), 7.46-7.51(2H, m), 7.71(1H, dd, J=7.3Hz and

7.2Hz), 7.90(1H, d, J=7.3Hz), 8.61(1H, br), 9.36(1H, br), 9.87(1H, brs).

Example 1129

5-Cyano-4,7-dihydro-4-phenyl-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride

The title compound was prepared from ethyl nipecotate, benzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 305(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.81-1.89(2H, m), 2.14-2.20(2H, m), 2.90-2.96(3H, m), 3.32-3.35(2H, m), 4.20(2H, br), 4.89(1H, s), 7.17-7.22(4H, m), 7.28-7.31(2H, m), 8.58(1H, br), 9.32(1H, br), 9.65(1H, brs).

Example 1130

5-Cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-4-(2-methylthiophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner as in Example 1003.

MS(EI): 366(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.58-1.66(2H, m), 1.83-1.89(2H, m), 1.97-2.02(2H, m), 2.15(3H, s), 2.50(3H, s), 2.62-2.65(1H, m), 2.84-2.87(2H, m), 5.32(1H, s), 7.12-7.30(5H, m), 9.57(1H, brs), 12.18(1H, brs).

Example 1131

5-Cyano-4-(2,6-dichlorophenyl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4-(2,6-dichlorophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine hydrochloride in the same manner as in Example 1003.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.52-1.56(2H, m), 1.83-1.87(2H, m), 1.99-2.06(2H, m), 2.15(3H, s), 2.52-2.55(1H, s), 2.83-2.87(2H, m), 5.90(1H, s), 7.17(1H, s), 7.28(1H, dd, J=7.3Hz and 7.2Hz), 7.36(1H, d, J=7.3Hz), 7.48(1H, d, J=7.3Hz),
5. 9.67(1H, brs), 12.12(1H, brs).

Example 1132

5-Cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-6-
10 (piperidin-4-yl)-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner as in Example 1003.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.57-1.62(2H, m), 1.83-1.86(2H, m),
15. 1.97-2.03(2H, m), 2.16(3H, s), 2.60-2.63(1H, m), 2.84-2.87(2H, m), 5.18(1H, s), 7.05(1H, s), 7.40-7.42(2H, m), 7.62-7.68(2H, m), 9.69(1H, brs), 12.23(1H, brs).

Example 1133

5-Cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-4-(2-nitrophenyl)-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner as in Example 1003.

MS(EI): 365(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.58-1.67(2H, m), 1.86-1.90(2H, m),
25. 1.99-2.06(2H, m), 2.16(3H, s), 2.58-2.61(1H, m), 2.86-2.90(2H, m), 5.36(1H, s), 7.26(1H, s), 7.42-7.48(2H, m), 7.69(1H, dd, J=7.3Hz and 7.2Hz), 7.88(1H, d, J=7.3Hz), 9.72(1H, brs), 12.26(1H, brs).

Example 1134

5-Cyano-4,7-dihydro-4-phenyl-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-4-

phenyl-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2
hydrochloride in the same manner as in Example 1003.

MS(EI): 319(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.54-1.57(2H, m), 1.81-1.87(2H,
5 m), 1.97-2.03(2H, m), 2.15(3H, s), 2.58-2.60(1H, m), 2.84-
2.86(2H, m), 4.87(1H, s), 7.17-7.20(4H, m), 7.27-7.32(2H, m),
9.52(1H, brs), 12.13(1H, brs).

Example 1135

5-Cyano-4-(2,2-difluoro-1,3-benzodioxol-4-yl)-4,7-dihydro-6-
10 propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl butanoate, 2,2-
difluoro-1,3-benzodioxol-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 1001.

MS(EI): 322(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.93(3H, t, J=7.3Hz), 1.63-
1.68(2H, m), 2.34-2.45(2H, m), 5.16(1H, s), 7.02(1H, d,
J=7.3Hz), 7.18(1H, dd, J=7.3Hz and 7.2Hz), 7.28(1H, d,
J=7.2Hz), 9.88(1H, brs), 12.22(1H, brs).

Example 1136

20 4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-
(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride

The title compound was prepared from ethyl nipecotate,
2,1,3-benzothiadiazol-4-aldehyde and 3-aminopyrazole in the
same manner as in Examples 1001 and 1002.

25 MS(EI): 363(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.89-1.98(2H, m), 2.22-2.29(2H,
m), 2.98-3.05(3H, m), 3.37-3.43(2H, m), 5.20(2H, br), 5.72(1H,
s), 7.24(1H, s), 7.48(1H, d, J=6.6Hz), 7.72(1H, dd, J=9.0Hz
and 6.6Hz), 7.99(1H, d, J=9.0Hz), 8.68(1H, br), 9.43(1H, br),
30 9.86(1H, brs).

Example 1137

5-Cyano-4-(2,2-difluoro-1,3-benzodioxol-4-yl)-4,7-dihydro-6-
(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

2 hydrochloride

The title compound was prepared from ethyl nipecotate, 2,2-difluoro-1,3-benzodioxol-4-aldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

5 MS(EI): 385(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.82-1.85(2H, m), 2.16-2.22(2H, m), 2.95-3.00(3H, m), 3.34-3.39(2H, m), 5.17(1H, s), 5.65(2H, br), 7.05(1H, d, J=7.3Hz), 7.19(1H, dd, J=7.3Hz and 7.2Hz), 7.29(1H, d, J=7.3Hz), 7.33(1H, s), 8.65(1H, br), 9.43(1H, br),
10 9.86(1H, brs).

Example 1138

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(piperidin-4-yl)-
15 2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner as in Example 1003.

MS(EI): 377(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.64-1.73(2H, m), 1.91-1.97(2H, m), 2.05-2.09(2H, m), 2.419(3H, s), 2.70-2.72(1H, m), 2.90-
20 2.93(2H, m), 5.71(1H, s), 7.22(1H, s), 7.45(1H, d, J=6.6Hz), 7.72(1H, dd, J=9.0Hz and 6.6Hz), 7.98(1H, d, J=9.0Hz), 9.71(1H, brs), 12.13(1H, brs).

Example 1139

25 5-Cyano-4-(2,2-difluoro-1,3-benzodioxol-4-yl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4-(2,2-difluoro-1,3-benzodioxol-4-yl)-4,7-dihydro-6-(piperidin-4-yl)-
2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner
30 as in Example 1003.

MS(EI): 399(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.5-1.58(2H, m), 1.86-1.90(2H, m), 1.99-2.03(2H, m), 2.16(3H, s), 2.59-2.62(1H, m), 2.85-

2.89(2H, m), 5.15(1H, s), 7.03(1H, d, J=7.3Hz), 7.17(1H, dd, J=7.3Hz and 7.2Hz), 7.26-7.31(2H, m), 9.71(1H, brs), 12.26(1H, brs).

Example 1140

5 5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride

The title compound was prepared from ethyl nipecotate, 2-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

10 MS(EI): 330 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.86-1.90(2H, m), 2.18-2.22(2H, m), 2.92-2.98(3H, m), 3.34-3.37(2H, m), 5.10(2H, br), 5.25(1H, s), 7.27(1H, s), 7.43-7.47(2H, m), 7.68(1H, dd, J=7.3Hz and 7.2Hz), 7.82(1H, d, J=7.3Hz), 8.61(1H, br), 9.41(1H, br),

15 9.93(1H, brs).

Example 1141

5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4-(2-cyanophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner as in Example 1003.

MS(EI): 344 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.58-1.63(2H, m), 1.82-1.87(2H, m), 1.98-2.06(2H, m), 2.16(3H, s), 2.59-2.61(1H, m), 2.84-2.88(2H, m), 5.23(1H, s), 7.25(1H, s), 7.39-7.46(2H, m), 7.6(1H, dd, J=7.3Hz and 7.2Hz), 7.81(1H, d, J=7.3Hz), 9.77(1H, brs), 12.26(1H, brs).

Example 1142

30 5-Cyano-4,7-dihydro-6-(piperidin-4-yl)-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine 3 hydrochloride

The title compound was prepared from ethyl nipecotate, pyridine-4-aldehyde and 3-aminopyrazole in the same manner as

in Examples 1001 and 1002.

MS(EI): 306(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.86-1.92(2H, m), 2.18-2.25(2H, m), 2.93-3.00(3H, m), 3.35-3.38(2H, m), 5.41(1H, s), 6.50(3H, br), 7.42(1H, s), 7.97(2H, d, J=6.8Hz), 8.90(1H, br), 8.93(2H, d, J=6.8Hz), 9.60(1H, br), 10.10(1H, brs).

Example 1143

5-Cyano-4,7-dihydro-6-(piperidin-4-yl)-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine 3 hydrochloride

10 The title compound was prepared from ethyl nipecotate, pyridine-3-aldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 306(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.86-1.93(2H, m), 2.19-2.25(2H, m), 2.90-2.97(3H, m), 3.35-3.38(2H, m), 5.39(1H, s), 6.50(3H, br), 7.41(1H, s), 8.09(1H, dd, J=8.2Hz and 5.4Hz), 8.49(1H, d, J=8.2Hz), 8.72(1H, br), 8.88(1H, d, J=5.4Hz), 8.92(1H, s), 9.57(1H, br), 10.02(1H, brs).

Example 1144

20 5-Cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-6-(piperidin-4-yl)-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine 3 hydrochloride in the same manner as in Example 1003.

25 MS(EI): 320(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.56-1.64(2H, m), 1.86-1.90(2H, m), 1.99-2.03(2H, m), 2.17(3H, s), 2.61-2.64(1H, m), 2.86-2.89(2H, m), 4.96(1H, s), 7.23(2H, d, J=6.8Hz), 7.31(1H, s), 8.50(2H, d, J=6.8Hz), 9.67(1H, brs), 12.25(1H, brs).

30 **Example 1145**

5-Cyano-4,7-dihydro-6-(1-methylpiperidin-4-yl)-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 5-cyano-4,7-dihydro-6-

(piperidin-4-yl)-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine 3 hydrochloride in the same manner as in Example 1003.

MS(EI): 320(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.57-1.60(2H, m), 1.84-1.89(2H, m), 1.99-2.05(2H, m), 2.17(3H, s), 2.58-2.61(1H, m), 2.85-2.8(2H, m), 4.98(1H, s), 7.29(1H, s), 7.35(1H, dd, J=8.2Hz and 5.4Hz), 7.55(1H, d, J=8.2Hz), 8.42-8.45(2H, m), 9.64(1H, brs), 12.23(1H, brs).

Example 1146

10 6-(exo-2-Azabicyclo[2,2,2]octan-6-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine
2 hydrochloride

The title compound was prepared from exo-2-azabicyclo[2,2,2]octane-6-carboxylic acid ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

MS(EI): 435(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.52-1.54(1H, m), 1.74-2.18(6H, m), 3.06-3.09(2H, m), 3.50-3.52(2H, m), 3.87(2H, br), 5.51(1H, s), 7.33(1H, d, J=7.3Hz), 7.55-7.60(2H, m), 7.84(1H, d, J=7.3Hz), 8.97(1H, br), 9.73(1H, br), 9.78(1H, brs).

Example 1147

25 6-(endo-2-Azabicyclo[2,2,2]octan-6-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine
2 hydrochloride

The title compound was prepared from endo-2-azabicyclo[2,2,2]octane-6-carboxylic acid ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1001 and 1002.

30 MS(EI): 435(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.67-1.69(3H, m), 2.02-2.12(4H, m), 3.02-3.05(1H, m), 3.31-3.35(1H, m), 3.45-3.51(2H, m), 4.04(2H, br), 5.50(1H, s), 7.34(1H, s), 7.56(1H, dd, J=7.3Hz

and 7.2Hz), 7.82(1H, d, J=7.3Hz), 8.16(1H, br), 9.82(1H, br), 9.93(1H, brs).

Example 1148

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(exo-2-methyl-2-azabicyclo[2,2,2]octan-6-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 6-(exo-2-azabicyclo[2,2,2]octan-6-yl)-4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 2 hydrochloride in the same manner as in Example 1003.

10 MS(EI): 449(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.42-1.45(1H, m), 1.72-1.88(5H, m), 2.06-2.09(1H, m), 2.46-2.51(4H, m), 3.04-3.07(1H, m), 3.45-3.48(2H, m), 5.48(1H, s), 7.34(1H, s), 7.57-7.60(2H, m), 7.83(1H, dd, J=7.3Hz and 7.2Hz), 9.83(1H, brs), 12.37(1H, brs).

15 **Example 1149**

Ethyl 4-(2,2-difluoro-1,3-benzodioxol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of 2,2-difluoro-1,3-benzodioxol-4-aldehyde (2.0 g), Meldrum's acid (1.6 g), ethyl 3-keto-hexanoate (1.7 g) and ammonium acetate (0.91 g) in acetic acid (20 mL) were stirred under reflux for 12 hrs. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give colorless crystals (2.4 g). To a solution of dimethylformamide (1.9 g) in chloroform (10 mL) were added 25 phosphorus oxychloride (4.0 g) and a solution of the obtained colorless crystals (2.4 g) in chloroform (10 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (27 g) solution was added, and the mixture was stirred for one hour. The reaction mixture 30 was extracted with chloroform, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals. To a solution

of the obtained colorless crystals in pyridine (20 mL) was added hydrazine (1.0 g), and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced
5 pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (190 mg) as colorless crystals.

MS(EI): 391 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.90-0.97 (6H, m), 1.58-1.64 (2H, 10 m), 2.60-2.64 (1H, m), 2.83-2.86 (1H, m), 3.83 (2H, q, $J=7.3\text{Hz}$), 5.32 (1H, m), 6.86 (1H, d, $J=7.3\text{Hz}$), 7.03-7.11 (2H, m), 7.24 (1H, s), 9.61 (1H, brs), 12.06 (1H, brs).

Example 1150

Ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate 2 hydrobromide
15

The title compound was prepared from 2-bromo-3-cyanobenzaldehyde in the same manner as in Example 1110.

MS(EI): 455 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.84 (3H, t, $J=7.3\text{Hz}$), 1.78- 20 1.81 (1H, m), 1.98-2.14 (3H, m), 2.87-2.90 (2H, m), 3.40-3.42 (2H, m), 3.78 (2H, q, $J=7.3\text{Hz}$), 3.80-4.25 (3H, m), 5.64 (1H, s), 7.35 (1H, s), 7.40-7.47 (2H, m), 7.70 (1H, d, $J=7.3\text{Hz}$), 8.10 (1H, br), 8.73 (1H, br), 9.37 (1H, brs).

Example 1151

Ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-(1-methylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate
25

The title compound was prepared from ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate 2 hydrobromide in the same manner as
30 in Example 1003.

MS(EI): 469 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO-d_6) δ (ppm): 0.85 (3H, t, $J=7.3\text{Hz}$), 1.53- 1.55 (1H, m), 1.70-1.72 (1H, m), 1.87-2.06 (4H, m), 2.16 (3H, s),

2.84-2.88 (2H, m), 3.78 (2H, q, J=7.3Hz), 3.94-3.96 (1H, m), 5.63 (1H, s), 7.34-7.48 (3H, m), 7.68 (1H, d, J=7.3Hz), 9.34 (1H, brs), 12.16 (1H, brs).

Example 1152

5 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methyl-2-oxo-piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 1-methyl-2-oxo-piperidine-4-carboxylic acid ethyl ester, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same
10 manner as in Example 1001.

MS(EI): 375 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.88-1.91 (1H, m), 2.26-2.33 (2H, m), 2.65-2.70 (1H, m), 2.82 (3H, m), 3.17-3.20 (1H, m), 3.31-3.36 (2H, m), 5.40 (1H, s), 7.29 (1H, s), 7.44 (1H, d, J=6.6Hz),
15 7.58 (1H, dd, J=9.0Hz and 6.6Hz), 7.92 (1H, d, J=9.0Hz), 9.88 (1H, brs), 12.22 (1H, brs).

Example 1153

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-methyl-2-oxo-piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from 1-methyl-2-oxo-piperidine-4-carboxylic acid ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 1001.

MS(EI): 437 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.88-1.92 (1H, m), 2.25-2.36 (2H, m), 2.69-2.74 (1H, m), 2.84 (3H, s), 3.18-3.36 (3H, m), 5.50 (1H, s), 7.37 (1H, s), 7.59-7.62 (2H, m), 7.85 (1H, d, J=7.3Hz), 9.90 (1H, brs), 12.33 (1H, brs).

Example 1154

30 4-(2-Chlorophenyl)-4,7-dihydro-5-(5-methyl-1,3,4-oxadiazol-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

A solution of 2-chlorobenzaldehyde (21 g), Meldrum's acid (21 g), 3-keto-hexanoic acid 2-cyanoethyl ester (27 g) and

ammonium acetate (13 g) in acetic acid (150 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give colorless crystals (16 g). A 1N NaOH solution (100mL) was added, and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was acidified. The reaction mixture was extracted with ethyl acetate, and the solvent was evaporated under reduced pressure to give colorless crystals (9.6 g). Hydrazine (0.22 g) and CDI (0.66 g) were added to the obtained colorless crystals (1.0 g) in DMF (5 mL), and the mixture was stirred for 3 hours. And the precipitated crystals were collected by filtration to give colorless crystals (0.7 g). Orthoacetic acid triethyl ester (3.7 g) was added to the obtained colorless crystals (1.0 g) in DMF (5 mL), and the mixture was heated for 3 hours. And the precipitated crystals were collected by filtration to give colorless crystals (0.6 g). To a solution of dimethylformamide (0.55 g) in chloroform (3 mL) were added phosphorus oxychloride (1.2 g) and a solution of the obtained colorless crystals in chloroform (6 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (7.7 g) solution was added, and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals. To a solution of the obtained colorless crystals in pyridine (10 mL) was added hydrazine (0.15 g), and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-

ethyl acetate (1:1)) to give the title compound (170 mg) as colorless crystals.

MS(EI): 356(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.00(3H, t, J=7.3Hz), 1.67-
5 1.74(2H, m), 2.31(3H, s), 2.70-2.83(2H, m), 5.71(1H, s), 7.07-
7.12(3H, m), 7.33-7.40(2H, m), 9.49(1H, brs), 12.04(1H, brs).

Example 1155

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(1-
(methylamino)ethyl)-2H-pyrazolo[3,4-b]pyridine

10 2 hydrochloride

The title compound was prepared from 2-methylglycine ethyl ester, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1015 and 1002.

MS(EI): 384(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.49(3H, d, J=7.3Hz), 3.09(3H, s), 4.00(2H, br), 4.60(1H, q, J=7.3Hz), 5.53(1H, s), 7.48-
7.53(2H, m), 7.64(1H, s), 7.82(1H, d, J=7.3Hz), 8.00-8.29(2H, br), 10.97(1H, brs).

Example 1156

20 4-(2-Chlorophenyl)-4,7-dihydro-5-(5-methyl-1,2,4-oxadiazol-3-
yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

A solution of 2-chlorobenzaldehyde (21 g), Meldrum's acid (21 g), 3-keto-hexanoic acid 2-cyanoethyl ester (27 g) and ammonium acetate (13 g) in acetic acid (150 mL) was heated
25 under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give colorless crystals (16 g). A 1N NaOH solution (100 mL) was added, and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room
30 temperature, and the solvent was acidified. The reaction mixture was extracted with ethyl acetate, and the solvent was evaporated under reduced pressure to give colorless crystals (9.6 g). An Ammonia solution (3.0 g) and CDI (2.8 g) were

added to the obtained colorless crystals (4.2 g) in DMF (20 mL), and the mixture was stirred overnight. The reaction mixture was extracted with ethyl acetate, and the solvent was evaporated under reduced pressure to give an oil. The residue
5 in N,N-dimethylacetamide dimethyl acetal (30 mL) solution was heated for 2 hours, and the solvent was evaporated under reduced pressure. Hydroxyammonium (1.4 g), 1N NaOH (20 mL), dioxane (20 mL) and acetic acid (28 mL) were added to the residue, and the mixture was heated for one hour. The reaction
10 mixture was extracted with ethyl acetate, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the colorless crystals (1.3 g). To a solution of dimethylformamide (1.7 g) in chloroform (10
15 mL) were added phosphorus oxychloride (3.5 g) and a solution of the obtained colorless crystals in chloroform (20 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (23 g) solution was added, and the mixture was stirred for one hour. The
20 reaction mixture was extracted with chloroform, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals. To a solution of the obtained colorless
25 crystals in pyridine (15 mL) was added hydrazine (0.6 g), and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-
30 ethyl acetate (1:1)) to give the title compound (500 mg) as colorless crystals.

MS(EI): 356(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.99(3H, s), 1.62(3H, t,

J=7.3Hz), 1.66-1.73(2H, m), 2.13(3H, s), 2.35-2.38(2H, m), 2.84-3.05(2H, m), 5.73(1H, s), 7.06-7.17(3H, m), 9.90(1H, brs), 12.11(1H, brs).

Example 1157

5 4-(2,1,3-Benzoxadiazol-4-yl)-4,7-dihydro-5-(5-methyl-1,3,4-oxadiazol-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde in the same manner as in Example 1154.

MS(EI): 364(M⁺).

10 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.01(3H, t, J=7.3Hz), 1.69-1.76(2H, m), 2.31(3H, s), 2.72-2.86(2H, m), 5.82(1H, s), 7.18(1H, d, J=6.6Hz), 7.32(1H, s), 7.48(1H, dd, J=9.0Hz and 6.6Hz), 7.80(1H, d, J=9.0Hz), 9.65(1H, brs), 12.07(1H, brs).

Example 1158

15 4-(2-Bromo-3-cyanophenyl)-4,7-dihydro-5-(5-methyl-1,3,4-oxadiazol-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-bromo-3-cyanobenzaldehyde in the same manner as in Example 1154.

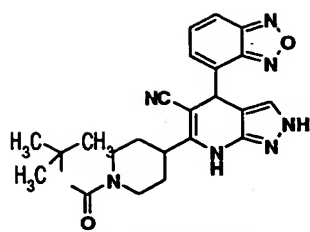
MS(EI): 425(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.00(3H, t, J=7.3Hz), 1.66-1.73(2H, m), 2.33(3H, s), 2.74-2.78(2H, m), 5.78(1H, s), 7.40-7.47(3H, m), 7.69(1H, dd, J=7.3Hz and 7.2Hz), 9.63(1H, brs), 12.14(1H, brs).

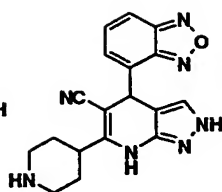
Example 1159

25 6-(1-Amino-1-methylethyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine hydrochloride

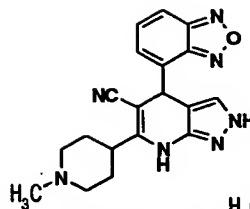
The title compound was prepared from 2,2-dimethylglycine ethyl ester, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Examples 1015 and 1002.



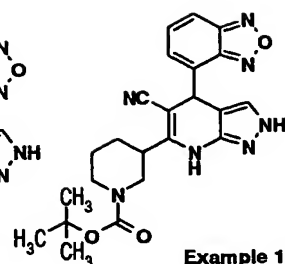
Example 1001



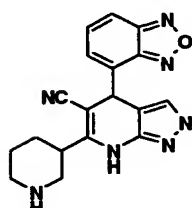
Example 1002



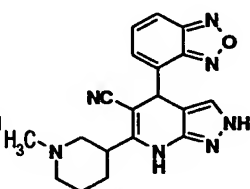
Example 1003



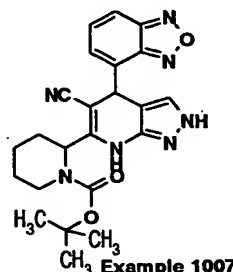
Example 1004



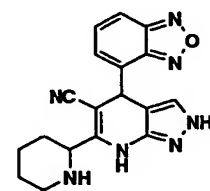
Example 1005



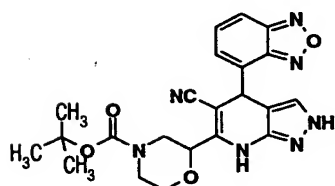
Example 1006



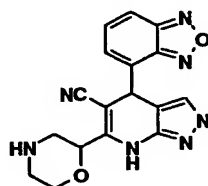
Example 1007



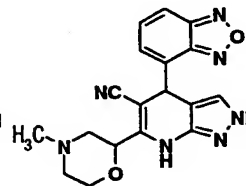
Example 1008



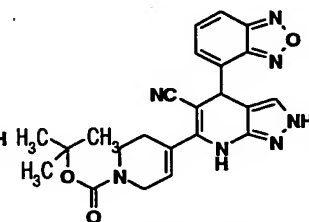
Example 1009



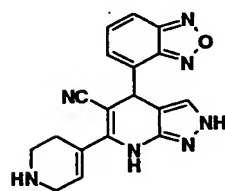
Example 1010



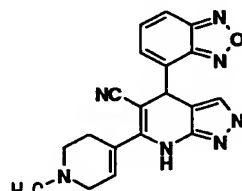
Example 1011



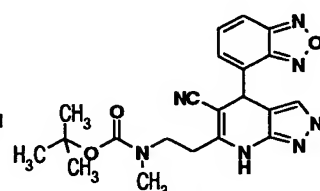
Example 1012



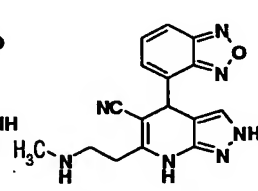
Example 1013



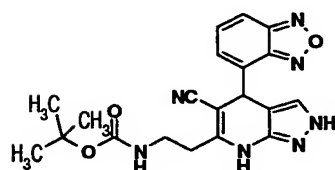
Example 1014



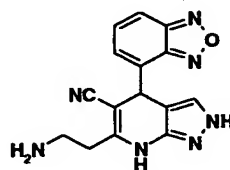
Example 1015



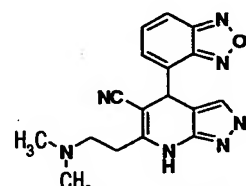
Example 1016



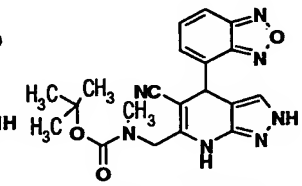
Example 1017



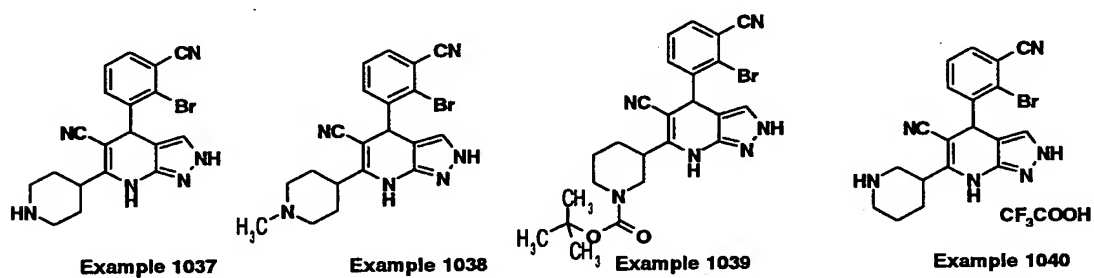
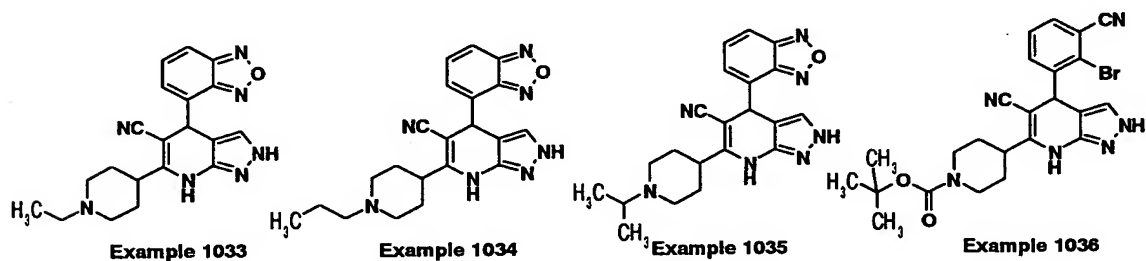
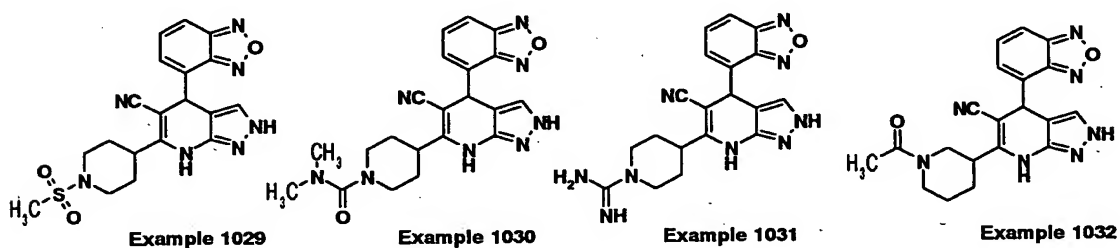
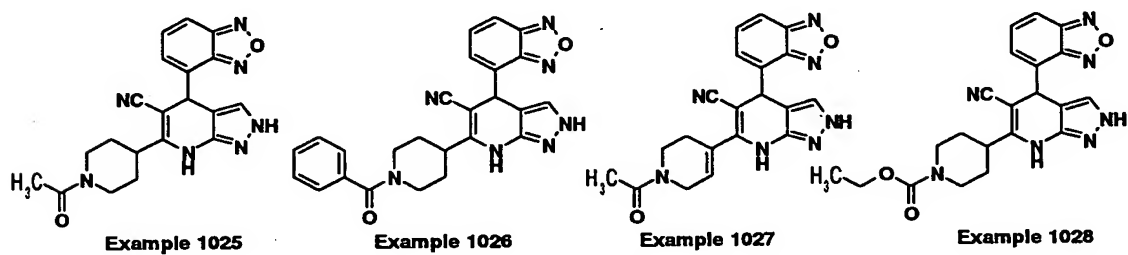
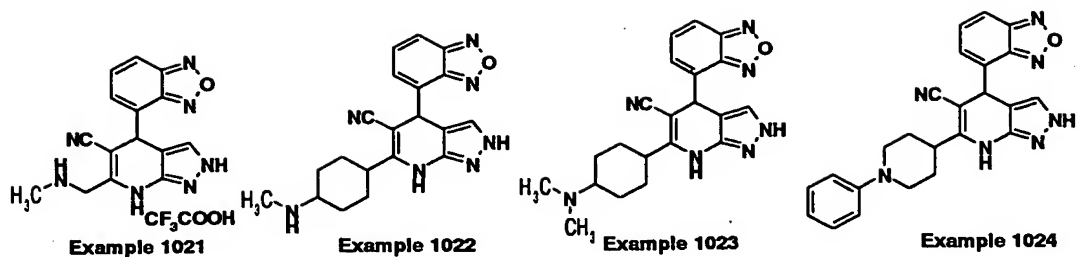
Example 1018

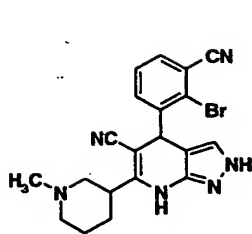


Example 1019

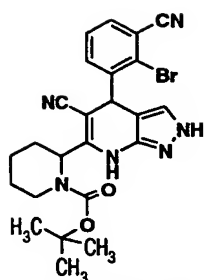


Example 1020

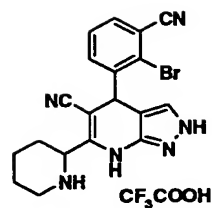




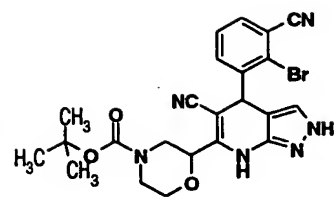
Example 1041



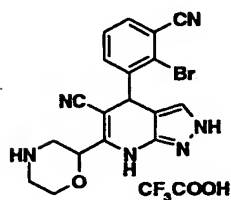
Example 1042



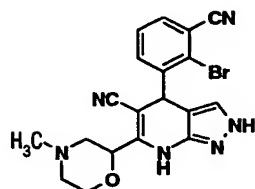
Example 1043



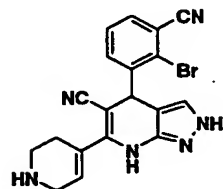
Example 1044



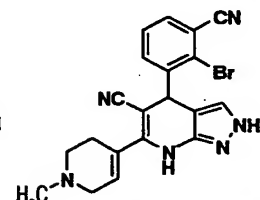
Example 1045



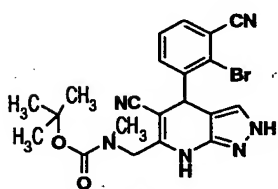
Example 1046



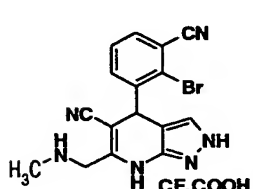
Example 1047



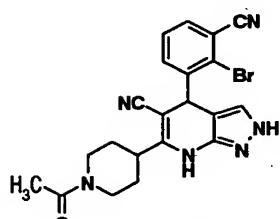
Example 1048



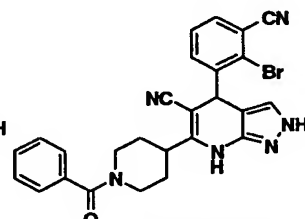
Example 1049



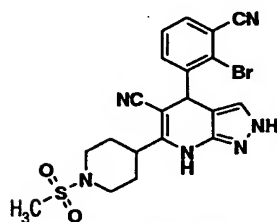
Example 1050



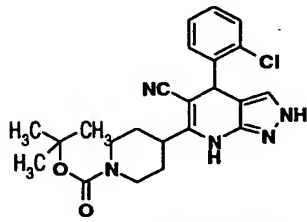
Example 1051



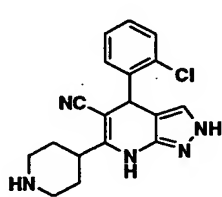
Example 1052



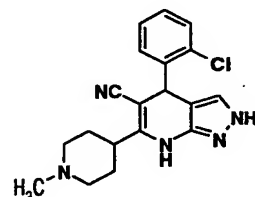
Example 1053



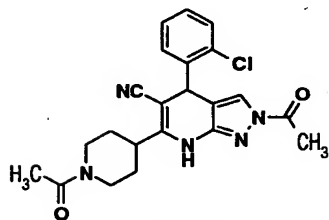
Example 1054



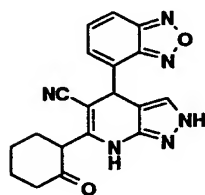
Example 1055



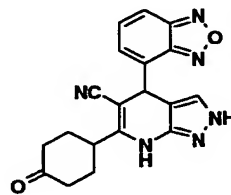
Example 1056



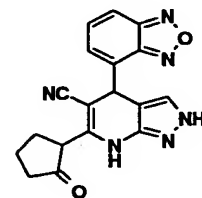
Example 1057



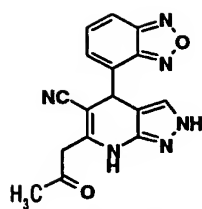
Example 1058



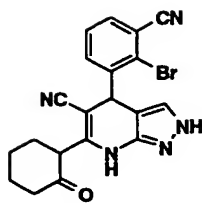
Example 1059



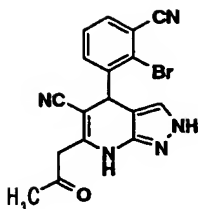
Example 1060



Example 1061



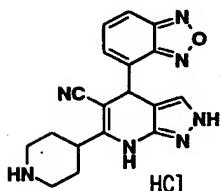
Example 1062



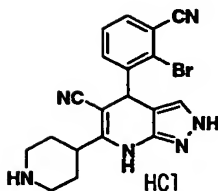
Example 1063



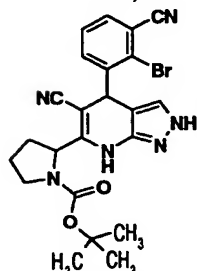
Example 1064



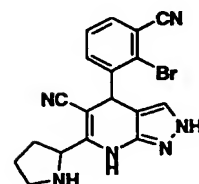
Example 1065



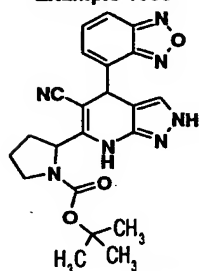
Example 1066



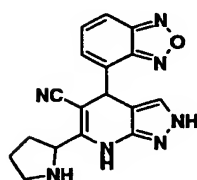
Example 1067



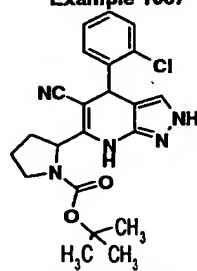
Example 1068



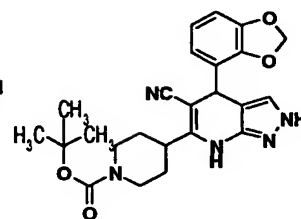
Example 1069



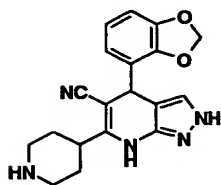
Example 1070



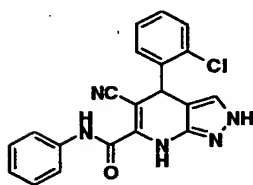
Example 1071



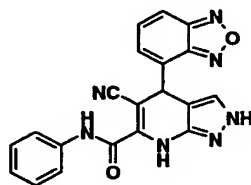
Example 1072



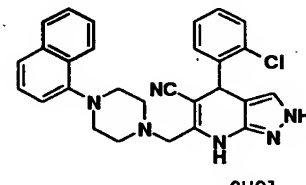
Example 1073



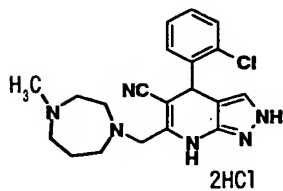
Example 1074



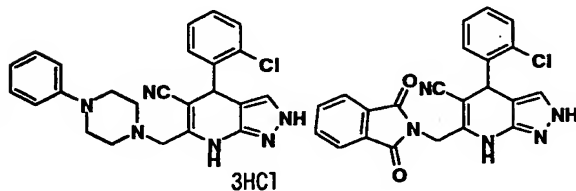
Example 1075



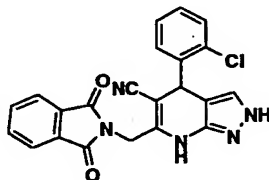
Example 1076



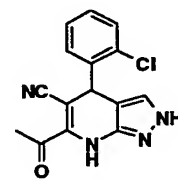
Example 1077



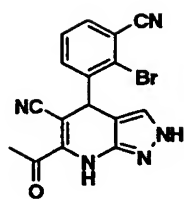
Example 1078



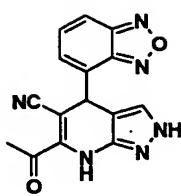
Example 1079



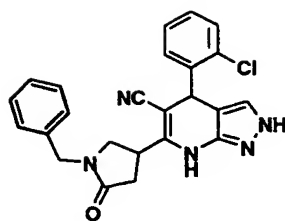
Example 1080



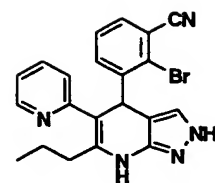
Example 1081



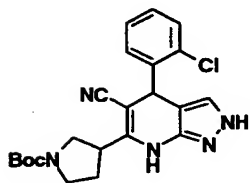
Example 1082



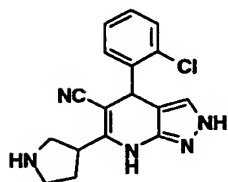
Example 1083



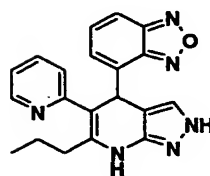
Example 1084



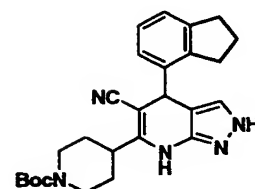
Example 1085



Example 1086



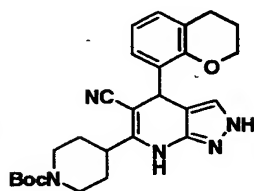
Example 1087



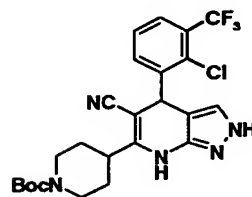
Example 1088



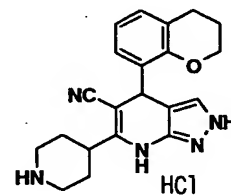
Example 1089



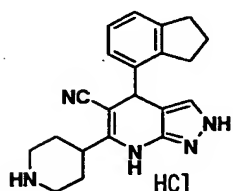
Example 1090



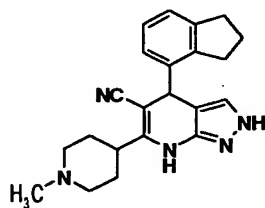
Example 1091



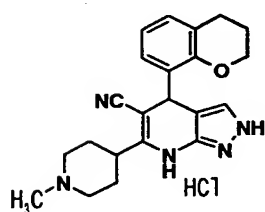
Example 1092



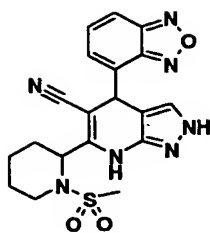
Example 1093



Example 1094



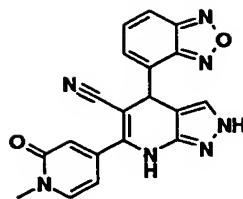
Example 1095



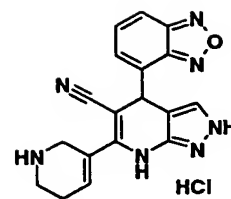
Example 1096



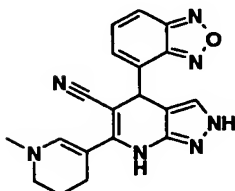
Example 1097



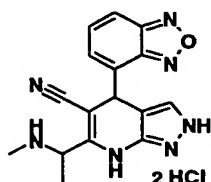
Example 1098



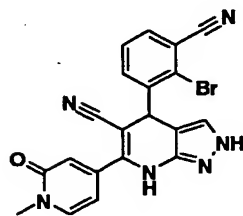
Example 1099



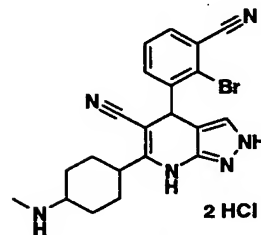
Example 1100



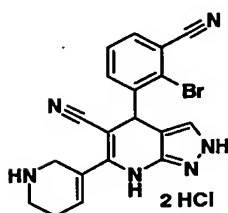
Example 1101



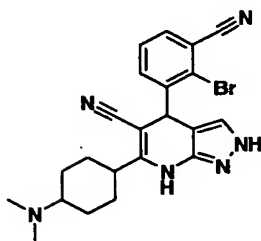
Example 1102



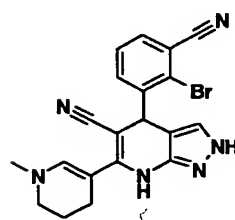
Example 1103



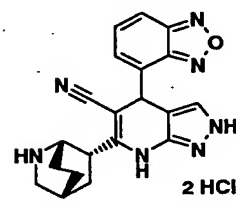
Example 1104



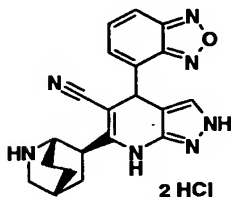
Example 1105



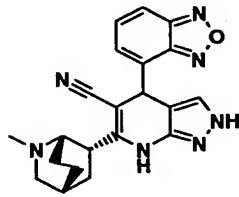
Example 1106



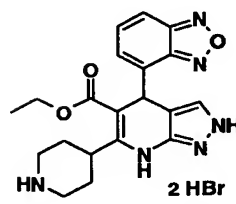
Example 1107



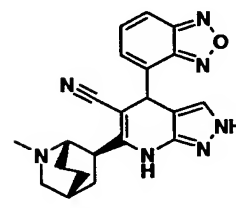
Example 1108



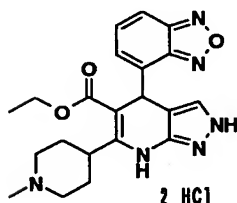
Example 1109



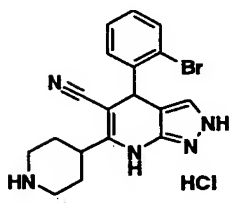
Example 1110



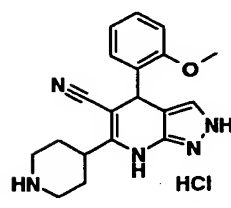
Example 1111



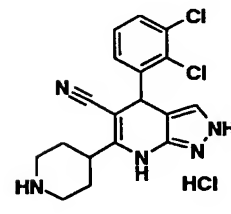
Example 1112



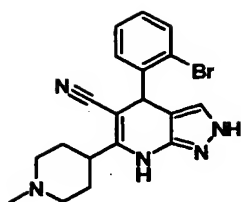
Example 1113



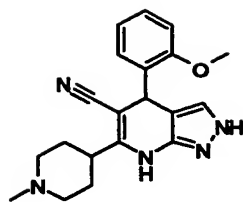
Example 1114



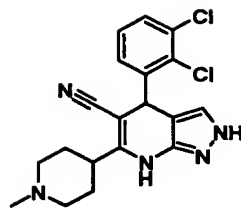
Example 1115



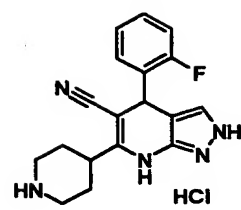
Example 1116



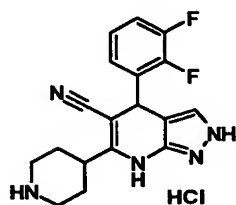
Example 1117



Example 1118



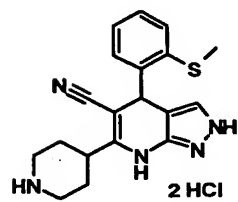
Example 1119



Example 1120



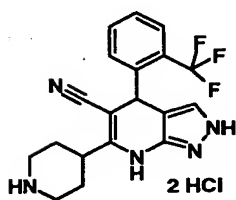
Example 1121



Example 1122



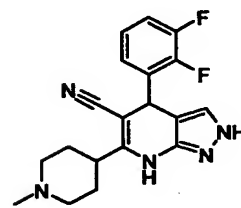
Example 1123



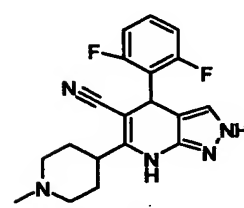
Example 1124



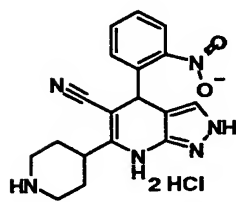
Example 1125



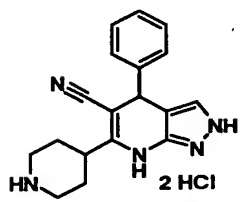
Example 1126



Example 1127



Example 1128



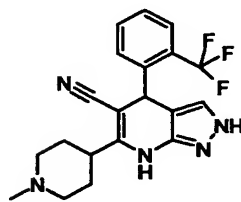
Example 1129



Example 1130



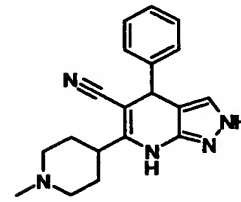
Example 1131



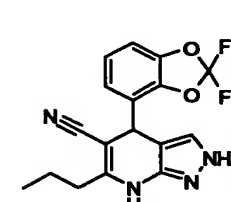
Example 1132



Example 1133



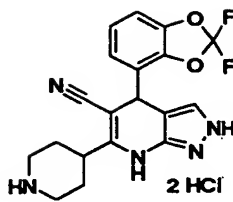
Example 1134



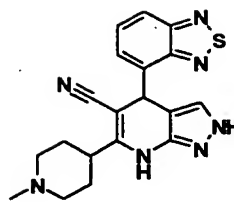
Example 1135



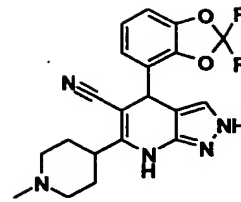
Example 1136



Example 1137



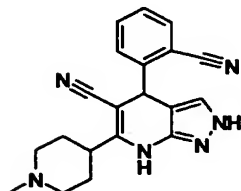
Example 1138



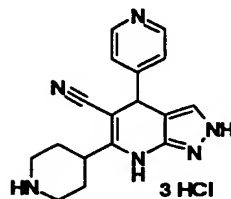
Example 1139



Example 1140



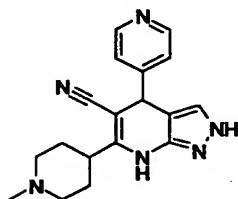
Example 1141



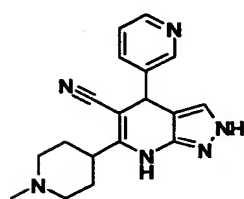
Example 1142



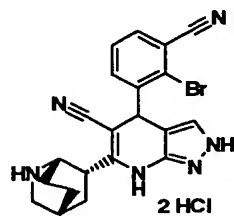
Example 1143



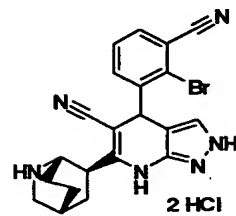
Example 1144



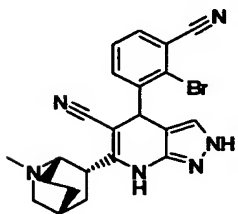
Example 1145



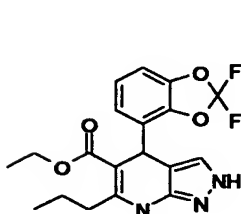
Example 1146



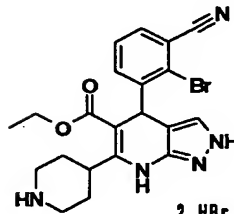
Example 1147



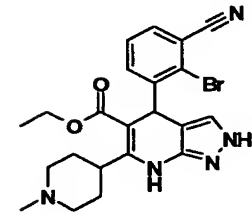
Example 1148



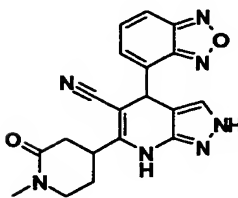
Example 1149



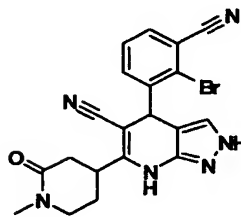
Example 1150



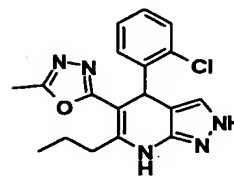
Example 1151



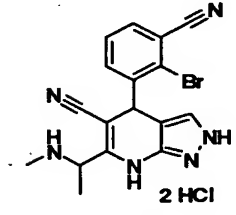
Example 1152



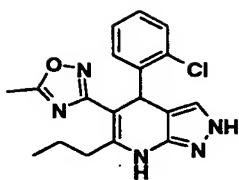
Example 1153



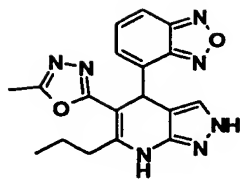
Example 1154



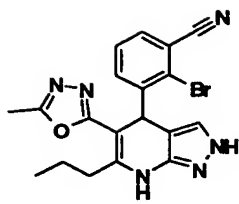
Example 1155



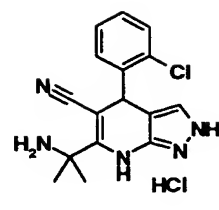
Example 1156



Example 1157



Example 1158



Example 1159

Formulation Example 1

The compound of Example 1 (0.5 part), lactose (25 parts), crystalline cellulose (35 parts) and corn starch (3 parts) were thoroughly mixed and kneaded well with a binder made of
5 corn starch (2 parts). The kneaded product was passed through a 16 mesh sieve, dried in an oven at 50°C and passed through a 24 mesh sieve. The kneaded powder thus obtained, corn starch (8 parts), crystalline cellulose (11 parts) and talc (9 parts) were thoroughly mixed and compression-punched to give tablets
10 containing 0.5 mg of the active ingredient per tablet.

Formulation Example 2

The compound of Example 1 (1.0 mg) and sodium chloride (9.0 mg) were dissolved in water for injection, and the solution was filtered to remove pyrogen. The filtrate was
15 transferred into an ampoule under sterile conditions. After sterilization, the ampoule was weld-sealed to give injection containing 1.0 mg of the active ingredient.

The effects of the compounds of the present invention on glycogen synthase kinase-3 beta (GSK-3 β) were evaluated and
20 confirmed as follows.

Formulation Example 3

The compound of Example 1001 (0.5 part), lactose (25 parts), crystalline cellulose (35 parts) and corn starch (3 parts) were thoroughly mixed and kneaded well with a binder
25 made of corn starch (2 parts). The kneaded product was passed through a 16 mesh sieve, dried in an oven at 50°C and passed through a 24 mesh sieve. The kneaded powder thus obtained, corn starch (8 parts), crystalline cellulose (11 parts) and talc (9 parts) were thoroughly mixed and compression-punched
30 to give tablets containing 0.5 mg of the active ingredient per tablet.

Formulation Example 4

The compound of Example 1001 (1.0 mg) and sodium chloride

(9.0 mg) were dissolved in water for injection, and the solution was filtered to remove pyrogen. The filtrate was transferred into an ampoule under sterile conditions. After sterilization, the ampoule was weld-sealed to give injection
5 containing 1.0 mg of the active ingredient.

The effects of the compounds of the present invention on glycogen synthase kinase-3 beta (GSK-3 β) were evaluated and confirmed as follows.

Experimental Example 1: GSK-3 β -inhibitory activity

10 CREB phosphopeptide (4.6 nmol), rabbit GSK-3 β (0.5 unit), ATP (5 nmol), [γ -³²P]ATP (12.3 kBq) and a test compound were reacted in a GSK-3 β buffer solution (25 μ L) (20 mmol/L Tris-HCl (pH 7.5), 10 mmol/L magnesium chloride, 5 mmol/L dithiothreitol) containing 1% dimethyl sulfoxide, at 30°C for
15 20 minutes. The reaction product (10 μ L) was adsorbed on a P81 ion-exchange paper, and the paper was washed with phosphoric acid (100 mmol/L) and measured for cpm on a scintillation counter. As a result, the compounds of the present invention showed the IC₅₀ values of 1 to 1000 nmol/L. For example, the
20 IC₅₀ values of the compounds of Examples 1, 14, 27, 66 and 140 were 210, 170, 25, 51 and 24 nmol/L, respectively.

CREB Phosphopeptide is Lys-Arg-Arg-Glu-Ile-Leu-Ser-Arg-Arg-Pro-Ser(P)-Tyr-Arg.

Experimental Example 2: GSK-3 β -inhibitory activity in rat
25 **cultured hippocampal neurons**

Hippocampal neurons were obtained from rat embryos on the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor), and
30 the culture was continued for 3 hours, whereby phosphorylation of Tau protein was induced. After the completion of culture, the level of phosphorylation of Tau protein was determined by EIA method using phosphorylated Tau-recognizing antibody

(phosphorylated site by GSK-3 β), and the inhibitory effect of the GSK-3 β inhibitor on the neurons was evaluated. Fig. 1 shows the GSK-3 β -inhibitory activity of the compounds of Example 47 and Example 137.

5 Experimental Example 3: Effect on amyloid β -induced cytotoxicity in rat cultured hippocampal neurons

Hippocampal neurons were obtained from rat embryos on the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β 10 (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor), and the culture was continued for 24 hours, whereby cytotoxicity (decreased activity of intracellular dehydrogenases) was induced. After the completion of culture, activity of intracellular dehydrogenases was determined and the effect of 15 the GSK-3 β inhibitor on the amyloid β -induced cytotoxicity was evaluated. Fig. 2 shows the effect of the compounds of Example 66 on amyloid β -induced cytotoxicity.

Experimental Example 4: GSK-3 β -inhibitory effect in gerbil brain ischemia model

20 A test compound (GSK-3 β inhibitor) was intraperitoneally administered to gerbils and 30 minutes later, brain ischemia was created by shutting off (for 4 minutes) all carotid arteries, whereby phosphorylation of Tau protein in the brain was induced. Three hours after the brain ischemia, the 25 hippocampus was obtained from the gerbil brain and the level of phosphorylation of Tau protein was determined by Western blot using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β), based on which the GSK-3 β -inhibitory effect of the GSK-3 β inhibitor in the gerbil brain 30 was evaluated. Fig. 3 shows the GSK-3 β -inhibitory effect of the compounds of Example 27 in gerbil brain ischemia model.

Experimental Example 5: GSK-3 β -inhibitory activity

CREB phosphopeptide (4.6 nmol), rabbit GSK-3 β (0.5 unit),

ATP (5 nmol), [γ - 32 P]ATP (12.3 kBq) and a test compound were reacted in a GSK-3 β buffer solution (25 μ L) (20 mmol/L Tris-HCl (pH 7.5), 10 mmol/L magnesium chloride, 5 mmol/L dithiothreitol) containing 1% dimethyl sulfoxide, at 30°C for 20 minutes. The reaction product (10 μ L) was adsorbed on a P81 ion-exchange paper, and the paper was washed with phosphoric acid (100 mmol/L) and measured for cpm on a scintillation counter. As a result, the compounds of the present invention showed the IC₅₀ values of 1 to 1000 nmol/L. For example, the IC₅₀ values of the compounds are shown in the following Table 1.

CREB Phosphopeptide is Lys-Arg-Arg-Glu-Ile-Leu-Ser-Arg-Arg-Pro-Ser(P)-Tyr-Arg.

Table 1

Example No.	IC ₅₀ (nmol/L)
1002	10
1003	2.5
1008	3.7
1011	14
1023	4.1
1058	1.8
1063	3.0
1146	0.61
1148	3.2
1155	2.2
1158	0.65

Experimental Example 6: GSK-3 β -inhibitory activity in rat cultured hippocampal neurons

Hippocampal neurons were obtained from rat embryos on the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor), and the culture was continued for 3 hours, whereby phosphorylation of Tau protein was induced. After the completion of culture, the level of phosphorylation of Tau protein was determined by

EIA method using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β), and the inhibitory effect of the GSK-3 β inhibitor on the neurons was evaluated.

Experimental Example 7: Effect on amyloid β -induced

5 **cytotoxicity in rat cultured hippocampal neurons**

Hippocampal neurons were obtained from rat embryos on the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor), and
10 the culture was continued for 24 hours, whereby cytotoxicity (decreased activity of intracellular dehydrogenases) was induced. After the completion of culture, activity of intracellular dehydrogenases was determined, and the effect of the GSK-3 β inhibitor on the amyloid β -induced cytotoxicity was
15 evaluated.

Experimental Example 8: GSK-3 β -inhibitory effect in gerbil brain ischemia model

A test compound (GSK-3 β inhibitor) was intraperitoneally administered to gerbils, and 30 minutes later, brain ischemia
20 was created by shutting off (for 4 minutes) all carotid arteries, whereby phosphorylation of Tau protein in the brain was induced. Three hours after the brain ischemia, the hippocampus was obtained from the gerbil brain, and the level of phosphorylation of Tau protein was determined by Western
25 blot using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β), based on which the GSK-3 β -inhibitory effect of the GSK-3 β inhibitor in the gerbil brain was evaluated.

30 The compounds of the present invention show a selective and strong inhibitory action on glycogen synthase kinase-3 beta (GSK-3 β), and are useful as medicaments for prevention and/or treatment of diabetes, diabetic complications,

neurodegenerative diseases (Alzheimer's disease, ischemic cerebrovascular disorders, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism, 5 postencephalitic Parkinsonism, boxer's encephalopathy, Parkinsonism dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease, manic-depressive psychosis and the like), alopecia, breast cancer, 10 non-small cell lung carcinoma, thyroid cancer, T or B-cell leukemia, and several virus-induced tumors, or as immunopotentiators.

This application is based on patent application Nos. 15 2001-304707, 2001-26379, 2001-081238 and 2002-230581 filed in Japan, the contents of which are hereby incorporated by reference.